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HYPOPARATHYROIDISM

THE TREATMENT OF CHRONIC CASES

R. H. FREYBERG, M.D.
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AND
M. A. ROBB, M.S.
ANN ARBOR, MICH.

Hypoparathyroidism may occur spontaneously, the so-called idiopathic variety; more frequently, however, it follows operation for the removal of part or all of the thyroid gland. During such an operation the parathyroid bodies may be injured, their blood supply may be interfered with or they may be accidently removed, and as a result of any of these mishaps a state of hypoparathyroidism may result. Fortunately, owing either to recovery from trauma to the glands or their blood supply or to hypertrophy of remaining parathyroid tissue, the state of hypoparathyroidism may be acute and easily managed, especially with the judicious use of parathyroid extract. However, not infrequently a state of postoperative hypoparathyroidism may exist and require constant treatment throughout the remainder of the patient's life.

Recently we have had an opportunity to study, extensively, two persons with chronic postoperative parathyroid tetany. Under carefully controlled conditions, we have measured the effect of various remedies frequently employed in the treatment of this condition. It is our purpose in this communication to present the data obtained and the principles of treatment suggested by this study, and to contribute an explanation for the "refractiveness" to parathyroid extract so frequently encountered when this hormone is injected over a period of time.

REPORT OF CASES

CASE 1.—L. R., a woman, aged 36, had a thyroidectomy in this hospital for exophthalmic goiter on June 24, 1929. The basal metabolic rate promptly fell to normal and has remained so ever since. June 28, 1929, tetany, with carpopedal spasm occurred. She was treated with parathyroid extract subcutaneously, and calcium lactate and very small doses of viosterol orally. Eight days later the concentration of calcium in the blood serum was 7.0 mg. per hundred cubic centimeters of serum, and it steadily increased until it was 10.7 mg. August 20, when she was discharged from the hospital. She was advised to eat a high calcium diet and to take 2 Gm. of calcium lactate orally, and 0.5 cc. of parathyroid extract, subcutaneously each day.

She continued to feel well until January 1930, when she contracted influenza. She ceased taking the parathyroid extract at this time. In October 1930 her finger nails dropped off. They soon regrew, but they dropped off on two more occasions. In November 1930 she noticed dimness of vision, which became progressively worse, owing to the formation of cataracts. In February 1931 she began having frequent attacks of tetany, and almost constant pain and stiffness of the muscles of the extremities. She was successfully treated, elsewhere, with a high calcium diet, 6 Gm. of calcium lactate, and 3 Gm. of ammonium chloride orally, and 1 cc. of parathyroid extract subcutaneously daily. She continued on this plan of treatment until October 1933, when she again came to the University Hospital complaining of muscle cramps and pain in the extremities. She exhibited a brisk Chvostek's sign. The serum calcium was 5.4 and the serum phosphorus 7.3 mg. per hundred cubic centimeters. She was treated with a high calcium diet, from 3 to 12 Gm. of calcium lactate and small amounts of viosterol orally and from 1 to 2 cc. of parathyroid extract subcutaneously each day. The improvement, however, was not as great as before and, on several occasions, injections of 10 per cent calcium gluconate were given intravenously to relieve painful muscle spasms. December 18 the serum calcium was 7.3 mg. per hundred cubic centimeters. The cataracts were removed and the patient was discharged, with the advice to continue the treatment instituted in the hospital.

In January 1934 dicalcium phosphate ($CaHPO_4$) was substituted for the calcium lactate. Within a few days tetany occurred, which disappeared when calcium gluconate was taken instead of dicalcium phosphate. She was relieved of severe cramps and spasms, although the muscles of the extremities were stiff much of the time, so that she could not use her hands and arms well.

She returned again in July 1934, complaining of muscle cramps. Chvostek's and Trousseau's signs were present. The serum calcium was 6.1 mg. per hundred cubic centimeters. She failed to improve satisfactorily when treated as she had been during the previous hospitalization. When she was discharged, Aug. 17, 1934, the serum calcium was only 6.2 mg. per hundred cubic centimeters.

At home she became progressively worse, so that it was necessary to inject calcium chloride intravenously on numerous occasions, to relieve tetany. Jan. 9, 1935, she returned to the hospital. Carpopedal spasm was so severe that she was unable to use the hands. Sitting in a chair would precipitate cramps of the leg muscles. Chvostek's and Trousseau's signs were marked. The serum calcium and phosphorus were 4.8 and 7.1 mg. respectively per hundred cubic centimeters. Again treatment with high calcium diet, parathyroid extract, calcium lactate and small amounts of viosterol did not cause satisfactory improvement.

METABOLISM STUDIES

March 6 a study of the calcium and phosphorus exchange and serum concentrations was begun. The patient was fed the same diet day after day until June 7. This diet was rich in calcium, since it included 1,500 cc. of milk daily; the calcium-phosphorus ratio was 1.36. After a period of adjustment to the diet, the observations appearing in chart 1 were made. The excretion of calcium and phosphorus is charted in three day periods. At the beginning of each period, blood was removed for serum calcium and phosphorus determinations. The methods used have been described in a previous communication.[1]

From the Department of Internal Medicine, University of Michigan Medical School.

The authors are indebted to Dr. L. H. Newburgh for many helpful suggestions given during the course of this study.

Read before the Section on Practice of Medicine at the Eighty-Seventh Annual Session of the American Medical Association, Kansas City, Mo., May 15, 1936.

1. Freyberg, R. H., and Grant, R. L.: A Study of the Calcium and Phosphorus Metabolism in a Verified Case of Pituitary Basophilism, Arch. Int. Med. 58: 213-228 (Aug.) 1936.

This study reveals the following significant facts: A high calcium diet (with 1,500 cc. of milk daily) alone caused no improvement. When 240 cc. of a 5 per cent solution of calcium lactate was taken there was a prompt rise in the serum calcium and a fall in serum phosphorus and distinct clinical improvement, with disappearance of tetany. The calcium lactate was then abruptly stopped, and inside of twenty-four hours the

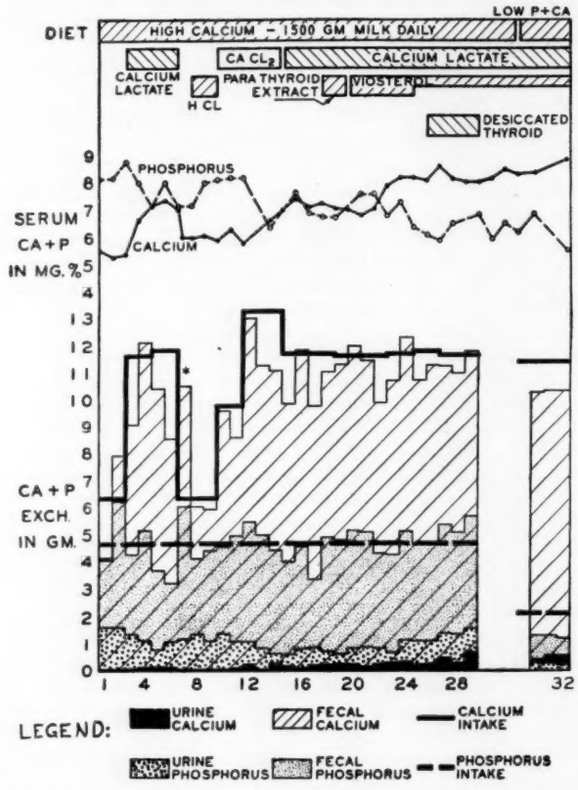

Chart 1.—Calcium and inorganic phosphorus metabolism during the first portion of the study of case 1. The exchange of these elements is represented by three day periods. Star indicates two days.

serum calcium had fallen to such a degree that the patient had a carpopedal spasm. Beginning with period 8, hydrochloric acid was given in large amounts with the hope that the absorption of calcium might be increased or that calcium would be liberated from the skeleton and thus raise the concentration of serum calcium. However, no benefit resulted. Beginning with period 10, a 10 per cent solution of calcium chloride was administered. It was thought that this acid-producing calcium salt not only would increase the calcium intake but might aid in absorption of calcium or in the liberation of this element from bony storehouses and would thus be of greater benefit to the patient than calcium lactate. When 30 cc. of this calcium chloride was given daily (supplying 1.16 Gm. of calcium), no benefit resulted. When the dose was doubled the serum calcium rose, but at a rate no greater than observed when less than the equivalent amount of calcium was supplied as calcium lactate; the serum phosphorus fell. The excretion of calcium in the urine increased, but there was no evidence of increased absorption. Calcium chloride was accordingly stopped, and 240 cc. of 5 per cent calcium lactate solution was given daily throughout the remainder of the first portion of this study.

Parathyroid extract was injected subcutaneously in 0.4 cc. doses daily through periods 18 and 19.[2] The patient was in no way benefited by it. Beginning with period 20, a large daily dose of irradiated ergosterol was administered. An especially concentrated solution[3] of viosterol was used, and an amount supplying 200,000 U. S. P. vitamin D units was given daily. There was a distinct rise in serum calcium and fall in serum phosphorus following this addition to the treatment. Beginning with period 25, the standard preparation of viosterol (250 D) was used, 3 cc. (30,000 U. S. P.) being given daily. No change occurred.

Desiccated thyroid, 0.2 Gm. daily, administered from period 26 through 29, had no distinct beneficial effect.

Study of the calcium and phosphorus exchange was discontinued after period 29. The patient continued to receive the same type of diet, 240 cc. of 5 per cent solution of calcium lactate and 2 cc. of viosterol daily until June 19, 1935. On this day the amount of calcium lactate was doubled. No significant change in serum calcium or phosphorus or in the clinical condition resulted.

June 29, milk was omitted from the diet. No other change was made. The diet was thus made comparatively poor in phosphorus and calcium, but with the calcium lactate medication the intake of calcium was high while that of phosphorus was low—the Ca/P ratio being 5.3. After a period of adjustment to this new diet, the calcium and phosphorus exchange was again studied. Chart 1 shows the decrease in serum phosphorus and the rise in serum calcium that occurred with the change in the Ca/P ratio of the ingesta.

The patient was discharged from the hospital on this last plan of treatment. She remained well at home, until October 10, when she returned for further study.

From October 21 to November 4 the patient was fed a diet made as low in phosphorus as possible while still keeping it adequate in other respects. (Egg albumin was used as the chief source of protein. The daily phosphorus intake was calculated to be about 0.4 Gm.). The serum phosphorus fell slightly and the calcium rose (chart 2). The diet was then changed again to the "low phosphorus" type previously used (omission of milk, chiefly).

Parathyroid extract was again injected subcutaneously, in doses larger than previously used, and again it was of no value.

After the patient recovered from an acute infection of the upper respiratory tract (which affected the calcium and phosphorus metabolism unfavorably), 1.8 Gm. of magnesium carbonate was given daily for two weeks. The serum phosphorus decreased and the serum calcium first increased and then fell. It was thought that the patient was not benefited by this medication.

The effect of parathyroid extract injected intravenously was next studied, in a manner similar to that used by Ellsworth.[4] While the patient was receiving nothing by mouth but 200 cc. of water hourly, the effect of 1 cc. of the drug was measured

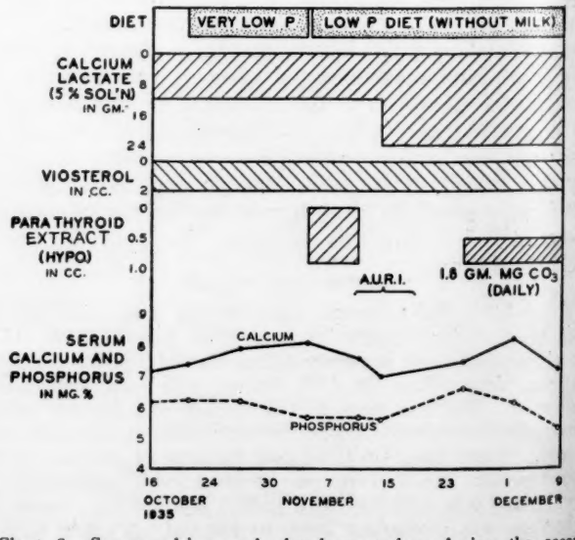

Chart 2.—Serum calcium and phosphorus values during the second part of study of case 1. A. U. R. I., acute upper respiratory infection.

by the quantity of phosphorus excreted hourly in the urine. Immediately after the drug was injected there was a distinct increase in urinary phosphorus, which continued through the four hour period of study (table 1). On the following day 4 cc. was injected intravenously. This amount caused almost

2. Throughout this paper, the dosage of parathyroid extract is expressed in cubic centimeters in order to avoid confusion that might result if the dosage were measured in units, since recently the unit strength of parathyroid extract has been changed.

3. Kindly supplied by the Winthrop Chemical Company.

4. Ellsworth, Read, and Nicholson, W. M.: Further Observations upon the Changes in the Electrolytes of the Urine Following the Injection of Parathyroid Extract, J. Clin. Investigation **14**: 823-829 (Nov.) 1935.

exactly four times the urinary excretion of phosphorus during the same interval of time as did 1 cc. on the previous day. The concentrations of calcium and phosphorus in the serum were not significantly changed following the first intravenous injection; after the larger dose the serum phosphorus was slightly lower, and the calcium also lower. Further study of the effect of parathyroid extract injected intravenously was not made, because almost immediately after the second injection the patient had a reaction characterized by faintness and

TABLE 1.—*Effect of Parathyroid Extract Injected Intravenously in Case 1* **

Date	Hour	Phosphorus in Urine, Mg.	Serum Calcium, Mg. %	Serum Phosphorus, Mg. %
12/ 9/35	6-7 a.m.	Trace		
	7-8	Trace		
	8-9	1	8.2	6.2
	9	1 cc. of parathyroid extract intravenously		
	9-10	9		
	10-11	9		
	11-12	6		
	12-1 p.m.	6		
		— (30)		
12/10/35	6-7 a.m.	}		
	7-8	} 4		
	8-9	}	8.2	6.4
	9	4 cc. of parathyroid extract intravenously		
	9-10	}		
	10-11	} 86		
	11-12	10		
	12-1 p.m.	32		
		— (128)		
	1-5	46		
	5-8	25		
12/11/35	8 a.m.	..	7.5	6.1

* The patient received nothing by mouth but 200 cc. of water hourly.

apprehension, rapid pulse and low blood pressure, followed by headache, extreme weakness and slight fever. Ten days later, severe generalized pruritus developed. This reaction was considered to be due to foreign protein. The parathyroid extract used was found to contain 0.4 per cent of protein by sulfosalicylic acid precipitation.

The effect of subcutaneous injections of parathyroid extract in amounts comparable to the intravenous doses was next tested in a similar way. The patient was fed a constant diet, in order that changes in phosphorus excretion might be significant. The urinary phosphorus decreased and the serum phosphorus increased during the period of therapy (table 2).

In January 1936 the last period of study was begun. A constant low phosphorus diet, a large amount of calcium lactate in 5 per cent solution, and 2 cc. of viosterol were given daily throughout this study. The daily urinary phosphorus excretion was measured in addition to the serum calcium and phosphorus determinations. It was observed (chart 3) that parathyroid extract injected intramuscularly was of no benefit. The effect of subcutaneous injections of a different preparation of parathyroid extract was then tested. The first trial seemed to benefit the patient. A subsequent trial showed it to be of no value, except possibly when given in very small doses. Later study showed that small doses also were valueless.

The disturbing effect of infection on calcium and phosphorus metabolism is again illustrated, especially during February 11-16, when the patient had a fever.

Lastly, the effect of frequent intravenous injections of calcium gluconate was tested. March 14, 9 cc. of a 10 per cent solution of calcium gluconate was injected twice daily, and on March 15 and 16, 10 cc. was injected three times daily. The serum calcium rose to only 8.4 mg. per hundred cubic centimeters and the serum phosphorus fell to 5.7 (chart 3). Most of the injected calcium was found in the urine of those days. In as short a time as four days most of the improvement was lost, illustrating the transient benefit of injected calcium salts.

CASE 2.—V. G., a woman, aged 35, had a thyroidectomy performed (elsewhere) in June 1929 for adenomatous goiter with hyperthyroidism. Following operation, progressive deafness and dimness of vision occurred, and her weight increased quite rapidly. In February 1930 tetany began. In June 1930 she began taking "two tablets" of thyroid extract (? 0.13 Gm.) daily and thereafter noticed an improvement, especially in hearing. Vision gradually became worse and the muscle spasms more frequent. Since early in 1932, treatment had consisted of a high calcium diet, a calcium salt orally and at times intravenously, and tablets of parathyroid extract. On this plan of treatment she had no severe spasms, although most of the time her muscles were so cramped and painful that she was incapacitated.

Feb. 15, 1935, she came to the University Hospital. Bilateral incipient cataracts and Chvostek's and Trousseau's signs were present. The serum calcium was 7.8 and phosphorus 6.1 mg. per hundred cubic centimeters. A high calcium diet and 12 Gm. of calcium gluconate daily relieved the severe muscle spasm. The cataracts were then treated, after which the following studies were made:

CALCIUM AND PHOSPHORUS STUDIES

Throughout the first period of study a high calcium diet (1,500 cc. of milk daily) was fed. Ten Gm. of calcium lactate powder was given daily from March 26 through April 9, without benefit (chart 4). A solution of calcium lactate, 240 cc. daily, was then given with no noticeable improvement. Sixty cc. of a 10 per cent solution of calcium chloride was next administered daily. A slight increase in serum calcium and no change in serum phosphorus resulted.

Beginning April 23, 240 cc. of 5 per cent solution of calcium lactate was given and also 3 cc. of viosterol (30,000 U. S. P. vitamin D units daily). There was a prompt increase in serum calcium and decrease in serum phosphorus, accompanied by clinical improvement. Doubling the amount of calcium lactate caused no added benefit. Beginning May 7, 0.4 cc. of parathyroid extract daily was injected subcutaneously. The increase in serum calcium and the clinical improvement were striking. (The serum phosphorus change could not be noted because the value at the beginning of this therapy was not known.) When the parathyroid extract was stopped the serum calcium promptly decreased and the phosphorus rose. These serum values changed toward the normal when the parathyroid extract was again injected.

Chart 4 shows the low level of basal metabolism that existed when no thyroid medication was given and the prompt increase resulting from the administration of desiccated thyroid. During this study no significant relationship between the serum calcium and phosphorus and the rate of basal metabolism or thyroid medication was observed.

TABLE 2.—*Ineffectiveness of Parathyroid Extract Injected Subcutaneously in Case 1 While a Constant Low Phosphorus Diet and a Constant Supply of Water Was Being Given*

Date	Parathyroid Extract Subcutaneously, Cc.	Phosphorus in Twenty-Four Hour Urine, Mg.	Serum Calcium, Mg. %	Serum Phosphorus, Mg. %
Dec. 16	None	60		
17	None	92		
18	None	76		
19	2.0	38	7.5	6.9
20	3.0	50		
21	4.0	26		
22	3.0	22		
23	None	23	7.9	7.1
24	None	12		

At the end of these studies the patient was discharged. She was advised to take a high calcium diet (1,500 cc. of milk daily), 240 cc. of 5 per cent solution of calcium lactate, 1 cc. of viosterol, 0.1 Gm. of desiccated thyroid orally, and 0.2 cc. of parathyroid extract, subcutaneously, daily. She remained in good health until December 1935, when she was unable to obtain all the medications (especially desiccated thyroid and frequently parathyroid extract). Muscle spasms and cramps recurred.

She returned to the hospital Jan. 27, 1936. Chvostek's and Trousseau's sign were present. Ten cc. of 10 per cent calcium

levulinate was injected intravenously for carpopedal muscle spasm. Further studies were carried out and are presented in chart 5.

She was fed a diet low in phosphorus and calcium (no milk) and 18 Gm. of calcium lactate in 5 per cent solution. No viosterol was given in order that the effect of parathyroid extract might be studied independent of any effect of this vitamin D concentrate. Parathyroid extract injected in 0.2 cc. doses subcutaneously during the first few days of study did

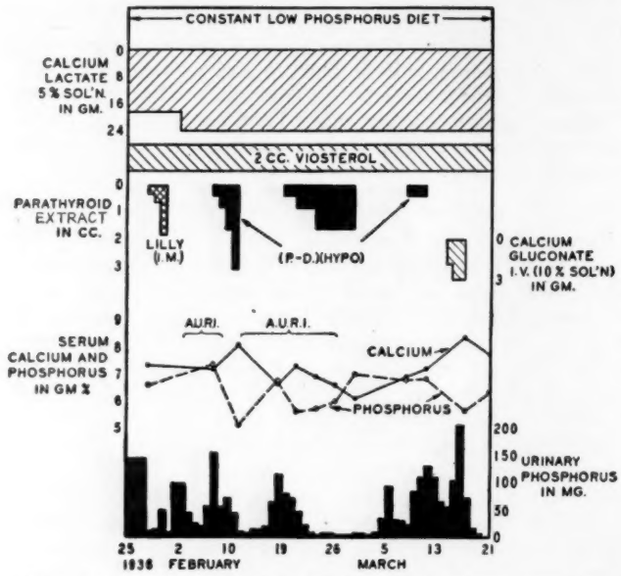

Chart 3.—Serum calcium and phosphorus and urinary excretion of phosphorus during the last period of study of case 1. A. U. R. I., acute upper respiratory infection.

not materially improve the patient, and it was thought that she might have become "refractive" to the extract. After a period without parathyroid extract, during which the serum calcium fluctuated around 8 mg. and the serum phosphorus rose slightly, it was found that 0.8 cc. of parathyroid extract daily injected subcutaneously caused a prompt increase in serum calcium and decrease in serum phosphorus, so that both values became normal within five days. When the amount of parathyroid extract was decreased, the serum calcium and phosphorus were again altered unfavorably. The patient was thus shown not to be refractive to the extract.

The same daily dose of parathyroid extract was then injected subcutaneously, in an amount sufficient to maintain the serum calcium and phosphorus values constant, and the calcium just at the low range of normal. Five Gm. of disodium acid phosphate in capsules was then fed daily, for five days. The serum calcium decreased. It appears that the administration of disodium acid phosphate diminished the 'effectiveness of the parathyroid extract.

The rise in serum calcium shown at the beginning of chart 5 might have been due to thyroid medication; but definite evidence that thyroid substance is of significant benefit to the calcium and phosphorus metabolism was not obtained later.

COMMENT

It should be noted that practically no calcium was excreted in the urine in case 1 when the serum level was below 7 mg. per hundred cubic centimeters (chart 1); at higher serum concentrations this element was excreted in normal amounts. This "threshold" phenomenon was found also by Albright and Ellsworth.[5]

Chart 3 shows the irregular excretion of phosphorus in the urine when the intake of this element was constant. We are unable to explain this.

The unfavorable influence of infection is repeatedly illustrated by case 1. In each case the menses were likewise found to have an unfavorable effect.

These studies serve admirably to indicate the considerations that are important in the treatment of chronic hypoparathyroidism. The data illustrate the benefit that is derived from certain remedies and point out certain things to be avoided if best results are to be obtained. Individual differences in patients naturally will govern details, but on the basis of observations made in these cases the fundamental principles for satisfactory treatment may be stated.

Diet.—It should be remembered that the serum of patients with hypoparathyroidism is characterized by a low concentration of calcium and a high level of phosphorus. To correct these abnormalities it is logical that the intake of calcium should be high and the intake of phosphorus low. To provide an abundant calcium intake it has been customary to prescribe a diet rich in calcium. The chief source of dietary calcium is milk, which is also rich in phosphorus; accordingly, all high calcium diets are high phosphorus diets. To provide a high calcium and low phosphorus intake, one must therefore feed a low phosphorus diet (which will also be relatively low in calcium) and supplement this with a calcium salt.

Albright [6] has produced evidence to show that the primary effect of parathyroid extract is on phosphorus, causing an increased excretion of this element in the urine; the effect on calcium appears to be secondary. It would naturally follow, then, that one should compensate for the most fundamental disturbance resulting from a lack of parathyroid hormone by providing a low intake of phosphorus. Further, if the phosphorus intake is kept low while the calcium intake is high, absorption of the latter element is facilitated.

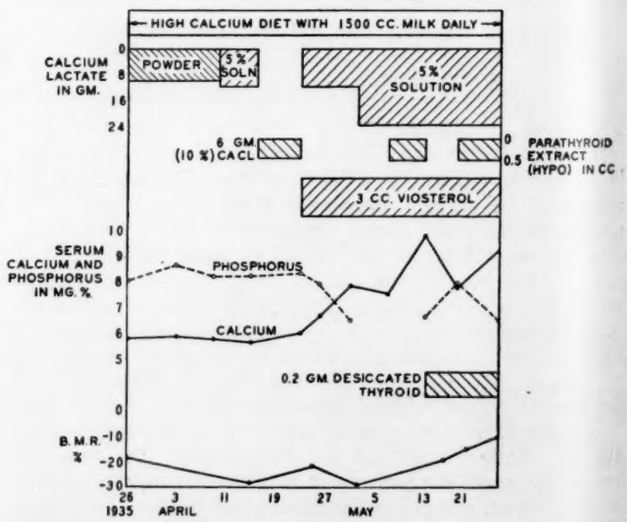

Chart 4.—Serum calcium and phosphorus levels and the basal metabolic rate during the first portion of study of case 2.

Shelling [7] has demonstrated the advantage of low phosphorus diets to parathyroidectomized rats. Shelling [8] and Ellsworth [9] have emphasized the importance of low dietary phosphorus in the treatment of parathy-

5. Albright, Fuller, and Ellsworth, Read: Studies on the Physiology of the Parathyroid Glands: Calcium and Phosphorus Studies in a Case of Idiopathic Hypoparathyroidism, J. Clin. Investigation **7**: 183-201 (June) 1929.

6. Albright, Fuller; Bauer, Walter; Ropes, Marion, and Aub, J. C.: Studies of Calcium and Phosphorus Metabolism: The Effects of the Parathyroid Hormone, J. Clin. Investigation **7**: 139-181 (April) 1929.

7. Shelling, D. H.: Calcium and Phosphorus Studies: Effect of Calcium and Phosphorus of Diet on Tetany, Serum Calcium, and Food Intake of Parathyroidectomized Rats, J. Biol. Chem. **96**: 195-214 (April) 1932.

8. Shelling, D. H., and Goodman, M. J.: Calcium and Phosphorus Studies: The Importance of Low Dietary Phosphorus in the Treatment of Parathyroid Tetany, J. A. M. A. **102**: 669-673 (March 3) 1934.

9. Ellsworth, Read: The Diagnosis and Treatment of Parathyroid Underfunction, Internat. Clin. **3**: 27-45 (Sept.) 1933.

roid tetany in human beings. The advantage of a low intake of phosphorus together with a high intake of calcium is repeatedly illustrated by our studies. When patient 1 took dicalcium phosphate instead of calcium lactate, tetany occurred. Again, when calcium lactate was abruptly stopped while the same high calcium diet continued (period 7, chart 1), tetany occurred within twenty-four hours, whereas later, when the diet was abruptly changed so as to lower markedly the phosphorus (and the calcium somewhat), and the same amount of calcium lactate continued, the patient was improved. In case 2 the unfavorable effect of disodium acid phosphate was observed (chart 5).

The diet can be made quite low in phosphorus by omitting milk. A still greater restriction of phosphorus can be obtained by omitting other foods rich in phosphorus (see food tables) and the avoidance of excess amounts of meat.

Calcium Medication.—An abundant intake of calcium is of the greatest importance. Except to relieve acute muscular spasm, the oral administration will suffice. For the reason already stated, calcium phosphate should not be used. Calcium lactate, gluconate and chloride are the salts most commonly employed. In our experience, calcium lactate gave results as good as or better than did the chloride, and it was less nauseating. From 12 to 18 Gm. of calcium lactate should be given daily; greater amounts were not found to be of added benefit. We feel that it is advantageous to give this medication in solution, in order to allow maximal absorption.

For the relief of acute muscular spasm, calcium should be injected intravenously. Ten cc. of a 10 per cent solution of the gluconate, levulinate or chloride injected slowly is usually sufficient.

Vitamin D.—Preparations of vitamin D have been reported to be without value by some investigators,[10] harmful by others,[9] and indispensable by still others.[11] Boothby[12] reports excellent results from the use of from two to three teaspoonfuls of cod liver oil (vitamins A and D) daily. Stacey[13] states that it is possible to maintain patients free from symptoms and with normal blood conditions with the use of large doses of pure vitamin D (calciferol).

In each of our patients there was definite benefit observed from the use of large doses of irradiated ergosterol (viosterol). The sharp change toward normal values for both serum calcium and phosphorus are especially well demonstrated by case 2 (chart 4). It must be emphasized, however, that for satisfactory results vitamin D should be given in large doses. In our tests, for a short time we administered 200,000 U. S. P. vitamin D units daily, although most of the time we used from 20,000 to 40,000 units. Other investigators[14] have used from 2 to 5 mg. of vitamin D (from 80,000 to 200,000 units) daily, with splendid results.

The manner in which vitamin D benefits these patients is not fully understood. Bauer, Marble and Claflin[14] have shown that vitamin D is effective only when the intake of calcium is high, and that its chief effect was to increase the absorption of calcium from the intestine. In case 1 the fecal calcium was not noticeably decreased by the administration of viosterol, so that in this patient vitamin D must have been effective in another way.

Acid Therapy.—Aub[15] has reported improvement in the tetany of hypoparathyroidism from the administration of hydrochloric acid or ammonium chloride. Acid-producing substances are known to liberate calcium from the readily available stores.[16] Recently, Campbell[17] has reported distinct benefit from the use of large doses of hydrochloric acid in two cases of postoperative tetany with achlorhydria. He states that the increase in serum calcium was due in part, at least, to increased absorption from the intestine. No benefit resulted from the use of hydrochloric acid to patient 1, who also had achlorhydria.

Calcium chloride has been recommended because of its twofold effect: a source of calcium and an acid-producing substance. In neither of our patients, however, was calcium chloride found to be of any advantage over an equivalent amount of calcium lactate, and it is more unpleasant to take.

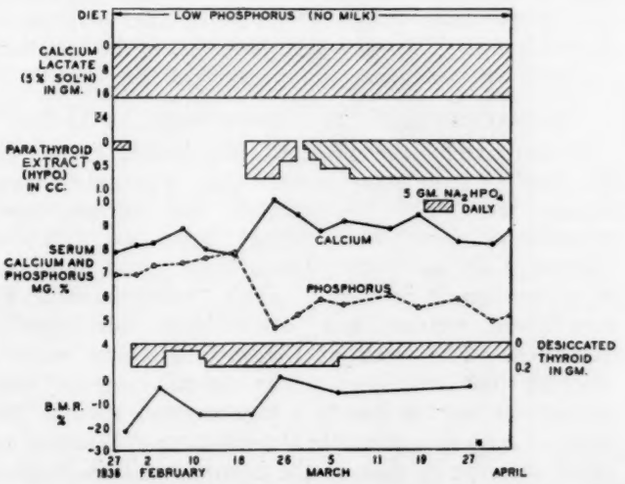

Chart 5.—Serum calcium and phosphorus levels and the basal metabolic rate during the second study of case 2.

Magnesium Salts.—Wenner[18] found that continuous oral administration of magnesium salts prevented tetany in parathyroidectomized animals. Ellsworth[19] administered magnesium carbonate to a patient with parathyroid tetany without striking benefit. In case 1 there was a rise followed by a fall in serum calcium and a decrease in serum phosphorus during the use of magnesium carbonate. We consider this salt to be of no value.

Thyroid.—Thyroid substance and thyroxine have been reported to exert a favorable effect on the disturbed calcium and phosphorus metabolism of hypo-

10. Findley, Thomas, Jr.: Failure of Irradiated Ergosterol to Relieve Parathyroid Tetany, Ann. Int. Med. **4**: 1144-1153 (March) 1931.
11. Boothby, W. M.: Treatment of Postoperative Parathyroid Insufficiency, Proc. Staff Meet., Mayo Clin. **10**: 87-91 (Feb. 6) 1935.
12. Boothby, W. M.; Haines, S. F., and Pemberton, J. deJ.: Postoperative Parathyroid Insufficiency, Am. J. M. Sc. **181**: 81-96 (Jan.) 1931.
13. Stacey, R. S.: Treatment of Low-Calcium Tetany with Calciferol, Lancet **2**: 656-658 (Sept. 21) 1935.
14. Bauer, Walter; Marble, Alexander, and Claflin, Dorothy: Studies on the Mode of Action of Irradiated Ergosterol in Hypoparathyroidism, J. Clin. Investigation **11**: 47-62 (Jan.) 1932. Stacey.[13]
15. Aub, J. C.; Albright, Fuller; Bauer, Walter, and Rossmeisl, Elsie: Studies of Calcium and Phosphorus Metabolism: In Hypoparathyroidism and Chronic Steatorrhea with Tetany, with Special Consideration of the Therapeutic Effect of Thyroid, J. Clin. Investigation **11**: 211-234 (Jan.) 1932.
16. Farquarharson, R. F.; Salter, W. T.; Tibbetts, D. M., and Aub, J. C.: Studies in Calcium and Phosphorus Metabolism: The Effect of the Ingestion of Acid-Producing Substances, J. Clin. Investigation **10**: 221-286 (June) 1931.
17. Campbell, David: The Treatment of Parathyroid Tetany, Lancet **1**: 369-372 (Feb. 16) 1935.
18. Wenner, W. F.: The Prevention of Tetany by Oral Administratin of Magnesium Lactate, Am. J. Physiol. **81**: 392-404 (July) 1927.
19. Ellsworth, Read: Observations upon a Case of Postoperative Hypoparathyroidism, Bull. Johns Hopkins Hosp. **52**: 131-144 (Feb.) 1933.

parathyroidism.[15] In case 1, in which the basal metabolism was normal, no benefit was derived from the use of desiccated thyroid. Thyroid substance improved patient 2 by correcting the hypothyroidism that existed, but that this drug was of benefit to the state of hypoparathyroidism is certainly not clearly shown. As a result of these observations we believe that thyroid substance should be used if hypothyroidism exists along with parathyroid tetany but that it is not particularly valuable otherwise.

Parathyroid Extract.—The most specific treatment for hypoparathyroidism is parathyroid extract, the use of which is true substitution therapy. Parathyroid extract injected subcutaneously or intramuscularly causes a prompt excretion of phosphorus in the urine and a lowering of the serum phosphorus, followed by an increase in serum calcium and the excretion of this element in the urine. In case 2, from 0.2 to 0.4 cc. of parathyroid extract daily, injected subcutaneously, caused the serum concentrations of calcium and phosphorus to become normal promptly. During the second period of study of this patient larger doses were necessary to maintain favorable serum calcium and phosphorus levels. This may have been due to the fact that viosterol was not being administered at this time.[20]

"REFRACTIVENESS" TO PARATHYROID EXTRACT

Unfortunately, the effect of parathyroid extract is completely lost in many persons after a period of continuous use. The subcutaneous and intramuscular injection of parathyroid extract from two different sources (Lilly and Parke, Davis & Co.) was shown to be of no benefit in case 1. This "refractiveness" to parathyroid extract has never been satisfactorily explained. The work of Collip,[21] to whom we are indebted for this therapeutic agent, suggests that refractivity may be due to a high concentration in the blood of a specific principle ("antihormone") having an effect opposite to that of the hormone. This investigator has very convincing evidence that the blood of animals injected chronically with certain pituitary fractions contains antagonistic substances which render these hormones ineffective. The existence of an antiparathyroid hormone, however, has not been demonstrated.

Although patient 1 was refractive to parathyroid extract injected subcutaneously or intramuscularly, similar amounts of the same preparation injected intravenously caused an immediate outpouring of phosphorus in the urine, an effect shown by Ellsworth [4] to be specific for this hormone. This behavior certainly shows that in refractive states the tissues on which the hormone acts to accomplish its effect are not at fault; on the other hand it shows that the extract, when injected subcutaneously or intramuscularly, does not get to these tissues in a potent state. That the hormone is rendered ineffective by substances in the blood stream appears unlikely, in view of the quantitative response to intravenous injections.

For parathyroid extract to be effective when injected subcutaneously or intramuscularly, it must be absorbed into the blood stream and carried in a potent state to the tissue on which it exerts its effect. If absorption from the tissues into which the extract is injected is interfered with, there will be a corresponding decrease or absence of effect. This may come about in a manner identical to that observed in the mechanism of local tissue immunity; i. e., with continued use of parathyroid extract, cells of the tissue into which it is injected may unite with hormone (just as cell products unite with antigens) and cause a localization of the hormone at the site of injection, where it is then destroyed. Fixation of the hormone at the site of injection, preventing absorption, would thus result in a state of "refractivity."

The occurrence in case 1 of an inflammatory reaction at the site of subcutaneous injection, much larger, warmer and more tender than resulted from injections of an equal amount of the extract in case 2, lends support to this explanation of the mechanism of "refractiveness."

Even though active when injected intravenously in patients otherwise refractive to parathyroid extract, this route of administration is not advised, because it is not practical and not without danger, as evidenced by our patient.

Many investigators urge that parathyroid extract be used in chronic hypoparathyroid states only for the relief of acute spasms, fearing the development of refractivity. When the disease can be controlled satisfactorily without its use, it would certainly seem wise so to do. The two subjects of this study could be sufficiently controlled without the use of parathyroid extract, so that they were free from tetany and enjoyed an active life. However, the serum calcium and phosphorus were never normal in patient 1, who was "refractive" to parathyroid extract, and in case 2 the concentrations of calcium and phosphorus in the serum were normal only when parathyroid extract was used. It is encouraging to note that the extract was apparently effective in case 1 for more than two and a half years, and in case 2 it was still effective after more than a year of almost continuous use.

SUMMARY AND CONCLUSIONS

Data obtained from extensive controlled studies on two patients with chronic postoperative hypoparathyroidism lead to the following statements regarding the treatment of this condition:

1. To compensate most satisfactorily for the altered state of calcium and phosphorus metabolism, the intake of phosphorus should be low and the calcium intake high. This can best be accomplished by feeding a low phosphorus diet (which will also be low in calcium) and large amounts of calcium salt, other than a phosphate. The commonly employed high calcium (milk) diet is undesirable because of its high phosphorus content.

2. A solution of calcium lactate, in amounts sufficient to provide from 1.5 to 2.5 Gm. of calcium daily, is in many respects the best method of administering calcium.

3. Vitamin D in large amounts is of definite value and should be given.

4. Hydrochloric acid and magnesium carbonate, as used, were not beneficial.

5. Thyroid substance should be administered, if hypothyroidism exists. Improvement in calcium and phosphorus metabolism that could be definitely attributed to thyroid medication was not observed.

20. Morgan, A. F., and Garrison, E. A.: Effect of Vitamin D and of Reaction of Diet upon Response to Parathyroid Extract, J. Biol. Chem. 85: 687-711 (Feb.) 1930.

21. Collip, J. B.: Recent Studies on Antihormones, Ann. Int. Med. 9: 150-162 (Aug.) 1935.

6. Although substitution therapy, consisting of the subcutaneous or intramuscular injection of parathyroid extract, is the most specific treatment, there are serious objections to the long continued use of this extract. If successful management can be accomplished without the use of parathyroid extract, it is advisable not to use it. These studies show that patients with severe chronic hypoparathyroidism can be maintained in a state of good, if not perfect, health by the treatment outlined, without the use of parathyroid extract.[22]

The effectiveness of parathyroid extract when injected intravenously into a patient who had become "immune" to the extract injected subcutaneously suggests that "refractiveness" to parathyroid extract is due to a localization and destruction of the active principle at the site of its injection.

ABSTRACT OF DISCUSSION

DR. W. M. KETCHAM, Kansas City, Mo.: I have been interested in parathyroid diseases for the last nine years, during which time I have seen four children with chronic parathyroid deficiency and five adults, all of the adults suffering as the result of a goiter operation. I was impressed with certain facts after watching these patients over a year or two. All of them had a blood calcium ranging from 5 to 7 mg., and all the adults had a cachexia. The adults presented a cachexic state in spite of the fact that they had had goiter operations and that one might have expected myxedema. They were disturbed at night with cramps in their legs, forcing them to get up and walk. They had night sweats, which were drenching. Associated with this was a marked muscular insufficiency, which interfered with their daily work, even mild housework. It was believed at first that these patients would be benefited promptly by the use of calcium, but in the majority of the cases there were no results with calcium glutinate or calcium chloride given by mouth or intravenously. In gastric analysis of four patients an achylia was discovered. Hydrochloric acid was added to the diet but satisfactory results from the administration of both the hydrochloric acid and the calcium were not obtained. Because of the cachectic condition, these patients were placed on large doses of vitamin D, and in all except one good results were obtained when this was combined with hydrochloric acid and calcium. When it was certain that these patients had hydrochloric acid, large doses of vitamin D and fairly large doses of calcium up to from 50 to 75 grains (3.25 to 5 Gm.) daily were given. No better results with the administration of thyroid extract combined with parathyroid extract or the latter alone were obtained than did the authors. In one case no results could be obtained with any treatment and the authors' explanation is probably a correct one. But I have felt that every patient suspected of having parathyroid deficiency should be given calcium, hydrochloric acid and large doses of vitamin D, combined with parathyroid extract both hypodermically and by mouth.

DR. WILLIAM J. KERR, San Francisco: I should like to ask how many international units of viosterol, or vitamin D, were given in these large doses. My reason for asking the question about viosterol is that recently an elderly physician by mistake took 2,300,000 international units of vitamin D daily for eighteen days, when he developed a nausea, anorexia, weakness, increased thirst and polyuria, and then passed into a coma and died. The total quantity of material used was 3 cc. a day. So far as I know, this is the first case of acute poisoning from vitamin D in man resulting in death. There are some chronic cases, but one should be very careful to specify how much vitamin D one is using. The widespread use of highly concentrated doses of irradiated ergosterol is dangerous. It is among the most potent drugs known. It should not be put into the hands of the public and should not be prescribed indiscriminately by physicians.

DR. R. H. FREYBERG, Ann Arbor, Mich.: I should wish to thank Dr. Ketcham for his discussion. It called to my mind several points. In reviewing the literature of the subject, I was struck with the relatively high incidence of hypoparathyroidism in women, especially in those cases which follow thyroidectomy. All our patients were women. Besides the unfavorable effect of infection on these patients, we have observed an unfavorable effect of menstruating on the calcium metabolism. Our first patient had achlorhydria, and I would point out that we did not measure any benefit to her from quite large amounts of hydrochloric acid, given along with a high calcium diet and no calcium salt. In reply to Dr. Kerr's question, at the beginning of the viosterol therapy we were using a preparation especially prepared for us by the Winthrop Chemical Company, which was ten times more potent than the usual preparation of viosterol. It was, in other words, 2,500 D. We gave amounts of this which were equivalent to from 160,000 to 200,000 U. S. P. units of vitamin D. That is a large dose. Our supply of that medication became exhausted, and throughout the remainder of the treatment we used the standard vitamin D, which was of the potency of 250 D, and we gave from 2 to 4 cc. of this preparation daily (from 20,000 to 40,000 U. S. P. vitamin D units). Since the data were compiled for this communication, we have had opportunity to treat two additional patients with chronic hypoparathyroidism following thyroidectomy, in the manner outlined, with splendid results.

22. Since these studies were made, we have had occasion to treat two other patients with chronic hypoparathyroidism, in the manner outlined, and the results have been excellent.

STUDIES IN SPLENOPATHY

INTRODUCTION

ALLEN O. WHIPPLE, M.D.
NEW YORK

This and the following three articles deal with work at the Combined Clinic in Splenopathy of the Vanderbilt Clinic and the Presbyterian Hospital. The members of the staff are Drs. Allen O. Whipple, Kenneth R. McAlpin, William P. Thompson, Louis M. Rousselot, Daniel N. Brown and Robert H. E. Elliott Jr.

At the Vanderbilt Clinic and the Presbyterian Hospital the splenopathies are studied by a group of physicians and surgeons. Those splenopathies associated with specific blood pictures are studied by the group interested in the anemias and leukemias. The group of splenopathies under consideration is followed by the physicians and surgeons of the Combined Clinic.

The Spleen Clinic is one of several Combined Clinics working at the Vanderbilt Clinic and the Presbyterian Hospital. These Combined Clinics, made up of medical, surgical, pathologic and in some clinics radiologic departments, are engaged in the study of the so-called middle ground diseases. The patients referred to these clinics are studied by the group together, therapy is agreed on and, whether medical or surgical, the results are studied and evaluated by the same group. The workers in these clinics, from whatever department they may be, speak the same language and see eye to eye, and there are no therapeutic or other miracles among friends. There, as in no other clinic, pride and prejudice disappear and an honest integration of opinions and convictions results.

The Combined Spleen Clinic was organized about six years ago. Before 1930 we saw an occasional splenopathy, but in both the medical and the surgical services we were rather complacent about the classification of splenic disease and were rather satisfied with our results. As a result of studying these diseases together

Read at a symposium on diseases of the spleen before the New York Academy of Medicine, April 2, 1936.

in a group made up of members of the medical and surgical staffs we know more about the diagnosis and therapy of some of these lesions but are less certain about others and acknowledge our inability to classify many of the splenopathies and their associated lesions. During the last six years we have had a steadily increasing number of these patients referred to us from the Vanderbilt Clinic as well as from the city and neighboring communities, so that in our files we now have studied and are seeing in our follow up some 200 patients with the lesions classified in the accompanying table.

In our surgical laboratory we have sections of 102 spleens, and the majority of these have been removed since the Spleen Clinic was organized.

From the standpoint of the care of the patient, teaching and research—the three cardinal criteria of any clinic worthy of the name—the Combined Clinic has everything to recommend it. Certainly the patients get more careful study and discriminating opinion as to therapy, because it is the result of agreement among medical and surgical workers, based on mutual follow-up studies. Overconservatism or radicalism in therapy cannot dominate such a clinic.

Classification of Total Cases Seen in the Spleen Clinic or by More Than One of its Members Since Its Organization Six Years Ago

Disease	Case
Total Cases	200
Banti's disease	47
Purpura	43
Hemolytic jaundice	46
Unclassified splenomegaly	24
Sickle cell anemia	4
Syphilis of spleen	4
Gaucher's disease	4
Polycythemia	3
Splenomegaly with colitis	2
Schistosomiasis	14
Cooley's anemia	3
Osteosclerotic anemia	1
Lymphosarcoma	1
Unexplained hypochromic anemia	1
Hodgkin's splenomegaly	3

From the standpoint of teaching, one has but to ask our best graduate students, working as residents or fellows, to get a convincing statement that no other place affords such a rare opportunity to study "middle ground" disease in all its phases. In view of the fact that within the next five years astonishing advances will be made in graduate teaching in all large metropolitan centers, as a result of the establishment of qualifying boards in medical specialties, this type of clinic will be in the greatest demand for graduate study and should and will be organized in all large clinics, especially in the university clinics.

Because the Combined Clinic attracts the able graduate student and stimulates inquiry, it is here that research, both clinical and laboratory, naturally develops. As an example of this I would call attention to the fact that it was the unexplained splenomegalies that stimulated this clinic to study experimentally portal bed obstruction and portal bed irritation. Experiments in schistosomiasis in monkeys in Puerto Rico, and in the portal areas of liver and spleen in other species in our surgical laboratory, are at present being studied and will be reported in subsequent communications from this clinic.

630 West One Hundred and Sixty-Eighth Street.

HEMOLYTIC JAUNDICE

ITS DIAGNOSIS, BEHAVIOR AND TREATMENT: A REVIEW OF FORTY-FIVE CASES

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The problem of the accurate diagnosis and subsequent treatment of patients presenting evidence of increased blood destruction with splenomegaly has long been of importance in medical and surgical clinics. Various criteria have been suggested for differentiating the various types of disturbances producing this syndrome, but considerable confusion still exists.

With the hope of obtaining a clearer understanding of the nature of this syndrome, the Spleen Clinic has been conducting a special study during the past six years. This study has resulted in a definite change in our point of view concerning diagnosis, indications for treatment and the therapeutic results that may be expected. Although much of that which follows has been said before, a difference in emphasis will be apparent.

During the past six years the Spleen Clinic has been able to study a total of forty-five patients presenting the clinical picture known as hemolytic jaundice. These cases have all been followed at regular intervals by this combined medical-surgical group; frequent laboratory tests have been made by technicians directly responsible to this clinic; separate records of each patient have been kept in our own files, as well as in the hospital record room; individual patients have been pursued, when pursuit was indicated, by our own social service worker, and nearly all splenectomies have been performed by our chief of clinic, Dr. Allen O. Whipple. With this method of study it has been possible to collect an enormous amount of data over extended periods of time with a degree of accuracy and uniformity difficult to obtain otherwise.

The term hemolytic jaundice has been used as a general diagnosis to include all patients presenting increased hemolysis of red cells within the body coincident with evidence of regeneration. In practice this definition is associated with variable jaundice and splenomegaly.

The Spleen Clinic, after many attempts to classify further the diseases causing this syndrome, has finally thought it wise to accept only two subdivisions. The first of these is a uniform, recognizable, curable entity: typical hemolytic jaundice. The second subdivision consists of a heterogeneous variety of disturbances grouped together under an intentionally vague term—the atypical hemolytic anemias.

TYPICAL HEMOLYTIC JAUNDICE

Typical hemolytic jaundice is, in our experience, a uniform and readily recognizable disease entity, provided certain diagnostic criteria are rigidly maintained. It is a chronic disease of long duration and of relative mildness. Acute exacerbations may occur, but these acute episodes are not common. The presenting symptom is chronic, variable jaundice and the outstanding physical finding is splenomegaly. A positive diagnosis is made in the laboratory. In all cases of typical hemolytic jaundice the peripheral blood contains the

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spherical microcytes that we believe are as pathognomonic of this disease as are the sickle cells in sickle cell anemia.

We in the Spleen Clinic have had the opportunity of studying thirty cases of this typical disease; of these thirty patients, eighteen have had their spleens removed. The more important clinical and laboratory data are presented in tables 1 and 2.

THE ATYPICAL HEMOLYTIC ANEMIAS

In marked contrast to typical hemolytic jaundice is our experience with the atypical hemolytic anemias. In the former group a definite diagnosis is promptly available, knowledge of the disease mechanism is accumulating, and the results of splenectomy can be predicted with security.

The atypical group comprises a total of fifteen cases presenting subacute or chronic acholuric jaundice, anemia with evidence of regeneration and splenomegaly. In all fifteen the possibility of typical hemolytic jaundice was considered, and in all fifteen this diagnosis could not be sustained because the blood failed to show the spherical microcytes with their attendant fragility changes.

In addition, the clinical behavior of this group, while under observation, showed differences from the typical cases, the behavior depending on the type of disturbance responsible for the hemolytic anemia.

Of the fifteen patients, three died with reticulum cell sarcomas of the spleen. These three patients were elderly and the disease progressed relentlessly to a fatal termination. Biopsy of affected superficial lymph nodes revealed the correct diagnosis in one. In the other two a diagnosis of atypical hemolytic anemia was all that could be sustained until autopsy revealed the neoplastic process. This type of hemolytic response to this type of neoplasm has been reported.[1]

Of the fifteen, two patients presented the syndrome of chronic hemolytic anemia in association with a fully positive Wassermann reaction. Treatment of their syphilis was followed by a cessation of the increased hemolytic activity, a regression in the size of the spleen and the amelioration of symptoms. Although hemolytic jaundice due to syphilis has been described, there is no available knowledge whatever concerning the mechanism.

Of the fifteen, one died of extensive caseating tuberculosis of the spleen and lymph nodes. Again the mechanism is not understood.

Of the fifteen, five are being followed at the present time. All five have chronic hemolytic anemia with jaundice, the etiology of which is quite unknown.

Splenectomy was performed in the remaining four. In two, operation resulted in no change in the activity of the hemolytic process. In the other two the hemolytic process progressed and the patients died and came to autopsy. There is nothing uniform in these four cases, they bear no resemblance to one another or to any other cases, and their diagnoses remain entirely obscure.

Details of eleven of this group appear in table 3.

In summary form, our clinical experience with this group of forty-five cases has led to the following tenets:

1. The syndrome of chronic variable acholuric jaundice, chronic variable anemia with regeneration and moderate to marked splenic enlargement, indicates the presence of a hemolytic process within the body.

2. Cases presenting this syndrome may be divided into two major groups:
   (*a*) Typical hemolytic jaundice.
   (*b*) The atypical hemolytic anemias.

3. The first symptoms of either group may have their onset at any age and in any race. There is no appreciable sex difference in the incidence.

4. Although a familial background of a similar process is somewhat more common in the typical hemolytic jaundice group, this family history may be present or absent in either group without affecting the diagnosis in any way. The former subdivision of cases into congenital and acquired types is therefore no longer valid.

5. Typical hemolytic jaundice is a clear cut definite disease entity, the diagnosis of which depends on the finding of spherical microcytes, with their attendant fragility changes, in the peripheral blood. Once the active phase of this disease is established it will continue, with fluctuations in intensity, until splenectomy is performed. The splenic pathologic changes are uniform and characteristic. Splenectomy results in an immediate cessation of the increased hemolytic activity with a prompt return of the blood values to normal. These brilliant results have been observed in all cases and persist without exception for as long as sixteen years after splenectomy.

6. The atypical hemolytic anemias comprise a heterogeneous group of disturbances that are associated with increased blood destruction and splenic enlargement. In some of our cases the primary disturbance has been neoplastic, in others infectious, in many unknown. Splenectomy is not indicated, for obvious reasons, in this group.

7. Correct clinical diagnosis before operation is therefore essential.

THE NATURE OF TYPICAL HEMOLYTIC JAUNDICE

The clinical study of patients with typical hemolytic jaundice before, during and after operation has led to certain conclusions concerning its behavior. Examination of the accompanying tables will show that there is no uniformity as to sex or racial distribution. The symptoms of chronic anemia with jaundice may appear at any age or an enlarged spleen may be found in an individual being examined for some unrelated complaint. The anemia may be mild or severe, or, in the latent cases, the blood count may be quite normal. The degree of jaundice varies likewise but is always proportional to the degree of anemia. The percentage of reticulocytes also varies within wide limits, depending, again, on the severity of the hemolytic process.

Although so many of the symptoms and signs of this disease appear to be variable, certain other features are uniform and constant. By observing the latter group of changes and by trying to understand their significance we have slowly come to a feeling of relative diagnostic security and confidence. In addition, these studies have helped materially in our understanding of the nature of this disease and how it works.

In every case of typical hemolytic jaundice the peripheral blood smear contains erythrocytes the diameter of which is obviously much less than normal but which in addition show no central pallor. In wet preparations these small cells appear spherical. With the micromanipulator these cells can be slowly and carefully examined and their spherical shape confirmed.

It is important that these cells should be detected and counted in wet film preparations with, when possible, the aid of the micromanipulator. Technics that give

1. Howard, Tasker: J. Lab. & Clin. Med. **14**: 1157 (Sept.) 1929.

the mean corpuscular volume may be misleading, as these spherical cells form only a small proportion of the total red cell colony, and many of the remaining cells, the reticulocytes, may be considerably larger than normal. In the presence of a high degree of reticulocytosis, mean corpuscular volume readings may be on the high side of normal and the spherical cells remain undetected.

The presence of these spherical cells in the blood of patients with typical hemolytic jaundice has been "discovered" by many observers, including myself. To Naegeli, however, belongs the credit for their original description; he suggested the possibility that these cells were responsible for the altered fragility to hypotonic salt solutions, which is such a constant finding. The work of Vallery-Radot on the relation between red cell

TABLE 1.—*Typical Hemolytic Jaundice—Nonsplenectomy* *

			First Blood Count										
Case	Age	Sex	Date	Hemoglobin, per Cent	Red Blood Cells, Millions	White Blood Cells	Neutrophils, per Cent	Reticulocytes, per Cent	Fragility	Microcytes, per Cent	Duration of Jaundice, Years	Spleen	Results
1	56	♀	2/26/22	35	2.8	5,000	77	Increased	0.55	Present	0.5	6 cm. below costal margin	Died 6/3/22, cause unknown
2	8 mo.	♂	3/ 2/28	26	2.4	35,400	22	10.0	0.60	?	6	8 cm. below costal margin	Left against advice
3	50	♀	11/15/29	68	3.2	5,300	59	15.5	0.525	Present	30	Enlarged	Symptoms continue, 38 yrs.
4	25	♀	6/ 8/31	41	3.1	6,700	70	24.0	0.675	33	20	26 cm. below costal margin	Symptoms continue, 25 yrs.
5	18	♂	7/14/31	78	4.1	9,000	66	10.6	0.575	Present	17	2 cm. below costal margin	Symptoms continue, 22 yrs.
6	14	♂	8/ 2/33	55	2.7	6,400	68	12.4	0.625	15	5	1 cm. below costal margin	Symptoms continue, 7 yrs.
7	31	♂	2/ 7/35	90	5.0	7,500	69	11.2	0.60	Present	20	2 cm. below costal margin	Symptoms continue, 20 yrs.
8	57	♀	7/ 3/35	57	3.4	5,000	40	10.9	0.625	11	25	To umbilicus	Symptoms continue, 8 yrs.
9	7	♀	9/25/35	68	4.1	13,200	61	17.8	0.65	7	4	To umbilicus	Symptoms continue, 4 yrs.
10	7	♂	9/25/35	74	3.6	12,200	43	13.6	0.65	9	4	7 cm. below costal margin	Symptoms continue, 4 yrs.
11	9	♂	9/25/35	60	3.3	7,900	51	14.5	0.65	12	5	8 cm. below costal margin	Symptoms continue, 5 yrs.
12	29	♀	9/18/35	85	4.0	8,400	77	12.0	0.65	16	9	9.5 cm. below costal margin	Symptoms continue, 9 yrs.

* All patients had anemia and were jaundiced.

TABLE 2.—*Typical Hemolytic Jaundice—Splenectomy* *

Case	Age	Sex	Date	Hemoglobin, per Cent	Red Blood Cells, Millions	White Blood Cells	Neutrophils, per Cent	Reticulocytes, per Cent	Fragility	Microcytes, per Cent	Duration of Jaundice	Splenectomy	Spleen	Pathology of Spleen	Pathology of Gallbladder	Duration of Follow Up	Results of Operation
13	18	♀	.....	..	...	.....	..	....	....	....	15 yrs.	4/10/20	Enlarged	Typical	Stones	16 yrs.	Excellent
First blood count			6/21/05	70	3.5	4,500	58	....	....	Many							
Last blood count			3/16/36	104	5.0	.....	..	1.1	0.475	13							
14	14	♂	.....	..	...	.....	..	....	....	....	18 yrs.	8/14/22	720 Gm.	Typical	No stones	13 yrs.	Excellent
First blood count			7/11/12	50	2.7	10,000	45	....	0.5+	Present							
Last blood count			5/15/35	108	5.7	.....	..	2.6	0.625	14							
15	4	♀	.....	..	...	.....	..	....	....	....	2 yrs.	9/28/25	Enlarged	Typical	?	4 yrs.	Died Aug. 1931, of poliomyelitis
First blood count			11/23/23	70	4.3	13,400	63	6.0	0.60	....							
Last blood count			12/12/29	80	5.2	.....	..	....	0.52	....							
16	35	♂	.....	..	...	.....	..	....	....	....	5 yrs.	6/ 4/26	1,032 Gm.	Typical	Stones	.....	Died 3 days postoperative
First blood count			6/ 2/26	70	3.7	5,400	66	....	0.55	....							
Last blood count			.....	..	...	.....	..	....	....	....							
17	28	♂	.....	..	...	.....	..	....	....	....	15 yrs.	11/ 8/29	675 Gm.	Typical	No stones	5 yrs.	Excellent
First blood count			11/ 3/29	60	5.1	7,300	63	0.9	0.425	....							
Last blood count			.....	..	...	.....	..	....	....	....							
18	25	♀	.....	..	...	.....	..	....	....	....	6 yrs.	6/23/25	475 Gm.	Typical	No stones	10 yrs.	Excellent
First blood count			9/ 8/24	75	3.8	8,100	74	15.0	0.58	Present							
Last blood count			4/15/36	94	5.1	.....	..	2.1	0.625	12							
19	8	♀	.....	..	...	.....	..	....	....	....	1 yr.	?/ ?/30	.....	.....	?	?	Record incomplete
First blood count			8/ 4/30	65	3.0	8,000	72	9.4	0.525	Present							
Last blood count			.....	..	...	.....	..	....	....	....							
20	45	♀	.....	..	...	.....	..	....	....	....	11 yrs.	10/23/30	970 Gm.	Typical	No stones	3.5 yrs.	Died Nov. 1934, carcinoma of rectum
First blood count			10/14/30	55	3.6	10,000	78	3.0	0.60	Present							
Last blood count			2/21/34	85	3.6	.....	..	4.3	0.575	Present							
21	26	♀	.....	..	...	.....	..	....	....	....	5 yrs.	6/15/31	1,460 Gm.	Typical	Stones	5 yrs.	Excellent
First blood count			4/23/31	42	2.4	8,900	67	15.4	0.575	Many							
Last blood count			5/ 6/36	109	4.9	.....	..	2.7	0.525	11							
22	20	♂	.....	..	...	.....	..	....	....	....	19 yrs.	?/ ?/20	.....	.....	?	3 yrs.	Excellent
First blood count			.....	..	...	.....	..	....	....	....							
Last blood count			3/10/32	98	4.9	.....	..	0.6	0.575	Present							
23	59	♀	.....	..	...	.....	..	....	....	....	15 yrs.	3/ 1/32	1,435 Gm.	Typical	No stones	10 mos.	Died 3/5/33, multiple sarcomatosis
First blood count			2/14/32	40	1.7	7,400	72	15.7	0.55	20							
Last blood count			6/ 8/32	82	4.7	.....	..	4.0	0.525	18							
24	28	♀	.....	..	...	.....	..	....	....	....	8 mos.	2/ 2/33	265 Gm.	Typical	No stones	3 yrs.	Excellent
First blood count			1/13/33	52	2.5	11,000	67	33.6	0.625	17							
Last blood count			5/ 5/34	..	4.4	.....	..	....	....	17							
25	48	♀	.....	..	...	.....	..	....	....	....	5 yrs.	?/ ?/27	Enlarged	.....	?	7 yrs.	Excellent
First blood count			?/ ?/25	35	...	.....	..	....	....	Present							
Last blood count			3/21/34	96	5.3	.....	..	2.7	0.50	8							
26	30	♂	.....	..	...	.....	..	....	....	....	9 days	3/19/34	750 Gm.	Typical	No stones	1 yr.	Excellent
First blood count			3/ 1/34	45	1.5	21,300	76	78.6	0.625	24							
Last blood count			9/19/34	98	4.4	.....	..	6.6	0.60	25							
27	35	♀	.....	..	...	.....	..	....	....	....	10 yrs.	5/25/34	1,000 Gm.	Typical	No stones	1 yr.	Excellent
First blood count			.....	..	...	.....	..	....	....	Present							
Last blood count			7/17/35	85	4.6	.....	..	1.7	0.575	16							
28	26	♂	.....	..	...	.....	..	....	....	....	4 yrs.	6/27/35	600 Gm.	Typical	No stones	6 mos.	Excellent
First blood count			5/15/35	90	4.6	6,300	64	10.7	0.625	9							
Last blood count			9/ 4/35	103	5.6	.....	..	0.9	0.65	5							
29	28	♀	.....	..	...	.....	..	....	....	....	18 yrs.	12/ 5/35	780 Gm.	Typical	No stones	2 mos.	Excellent
First blood count			11/18/35	83	3.7	17,300	79	17.6	0.70	15							
Last blood count			1/15/36	96	5.0	.....	..	0.5	0.65	15							
30	11	♀	.....	..	...	.....	..	....	....	....	11 yrs.	11/27/35	685 Gm.	Typical	No stones	2 yrs.	Excellent
First blood count			11/16/35	70	3.5	12,950	70	21.5	0.475	Present							
Last blood count			12/18/35	105	5.1	.....	..	7.3	0.575	21							

* All patients had anemia and were jaundiced.

diameter and fragility to hypotonic salt is of sufficient interest to warrant the presentation again of his table (table 4).

It was not until the recent work of Haden [2] appeared, however, that this relationship between shape, size and hemolysis was conclusively proved. His work leaves no doubt about the fact that these spherical cells are alone responsible for the fragility changes seen in all cases of typical hemolytic jaundice.

In addition, evidence is available to suggest a serious consideration of the importance of these spherical cells in the production of the active disease process.

This chain of evidence, although fragmentary in places, can be presented in order:

1. The fact can be accepted that all patients with typical hemolytic jaundice, as well as their relatives with the latent disease, have these spherical microcytes circulating in the peripheral blood. These abnormal cells constitute from 10 to 25 per cent of the total number of erythrocytes, the remaining cells being either reticulocytes or normal red blood cells. We have never observed reticulation in the spherical cells.

2. These spherical cells are directly responsible for the fragility changes to hypotonic salt solution.[2]

3. These spherical cells appear to be selectively removed from the general circulation by the spleen, where they are found in larger numbers than in the peripheral blood.

Sample Observation: A. H., an American woman, aged 28, with chronic anemia and jaundice, had a red blood cell count of 2,500,000; hemoglobin 52 per cent, reticulocytes 33 per cent, and fragility beginning at 0.625 per cent of sodium chloride. The spleen was moderately enlarged. There were no gallstones. Splenectomy was performed by Dr. Whipple in February 1933. The patient recovered promptly and has been entirely well since operation. Sections of the spleen are typical of hemolytic jaundice.[3]

At operation the following data were obtained: spherical microcytes in splenic arterial blood, 10.4 per cent; spherical microcytes in splenic vein blood, 8.4 per cent; spherical microcytes in splenic pulp, 48.0 per cent.

A small fragment of spleen is washed carefully in warm physiologic solution of sodium chloride to remove the excess blood. The fragment is then ground in a watch glass with a few drops of the patient's serum, smears are made and the proportion of spherical cells are counted.

4. There is enough evidence, I believe, to warrant the assumption that all the increased red blood cell destruction that results in the active phase of the disease takes place within the spleen. Some of this evidence is direct; most of it is inferred.

Direct evidence can be procured only by measuring the serum bilirubin concentrations in the blood of the splenic artery and vein at the time of operation. Obvious technical difficulties interfere with the collection of the necessary specimens. In spite of these difficulties we have found that the blood of the splenic vein contains more pigment than does the blood of the splenic artery.

These observations are in accord with the figures obtained by Rich and Rienhoff [4] in an active case of hemolytic jaundice and show that the spleen is actively destroying erythrocytes.

Indirect evidence concerning the activity of the spleen in this disease can be procured by observing the effects

TABLE 3.—*Atypical Hemolytic Anemia* *

Case	Age	Sex	First Blood Count: Date	Hemoglobin, per Cent	Red Blood Cells, Millions	White Blood Cells	Neutrophils, per Cent	Reticuleocytes, per Cent	Fragility	Microcytes	Duration of Symptoms	Splenectomy	Spleen	Pathology of Spleen	Pathology of Gallbladder	Duration of Follow-Up	Results
Cases in Which Splenectomy Was Performed																	
31	24	♀	3/ 1/20	50	4.7	6,700	62	1.0	0.55	0	4.5 yrs.	12/ 6/24	397 Gm.	Normal	No stones	15 yrs.	Improved; diagnosis unknown
32	27	♂	7/31/29	20	0.94	31,200	80	19.0	0.425	0	4 days	10/25/29	540 Gm.	Marked blood formation	Stones	1 yr.	Died 10/4/30; autopsy; acute course partly arrested; diagnosis unknown
33	63	♂	9/19/31	35	1.3	3,300	78	37.0	0.425	0	4 wks.	10/31/31	680 Gm.	Marked blood formation	No stones	1 mo.	Died 12/5/31; autopsy; splenectomy no help; diagnosis unknown
34	16	♂	6/23/33	80	3.9	10,000	59	5.7	0.425	0	11 yrs.	6/28/35	540 Gm.	Not typical	No stones	9 mos.	Situation 9 mos. post-operative unchanged
Cases in Which Splenectomy Was Not Performed*																	
35	55	♀	3/31/26	75	4.3	7,000	65	Not done	0.65	0	1 mo.	None	Palpable	.....	.....	.....	Jaundice disappeared; diagnosis unknown
36	44	♀	8/ 4/28	15	0.61	10,400	74	25.0	.....	0	6 mos.	None	580 Gm.	Sarcoma	.....	.....	Died 8/6/28; autopsy; sarcoma of spleen
37	56	♂	9/20/29	35	1.5	7,700	88	6.4	0.425	0	2 mos.	None	1,300 Gm.	Sarcoma	Normal	.....	Died 10/23/29; autopsy; sarcoma of spleen
38	6	♂	2/14/30	50	3.3	16,400	75	25.0	0.375	0	2 yrs.	None	9 cm. below costal margin	.....	.....	.....	Follow-up appointment not kept
39	72	♀	1/15/32	48	1.8	6,500	76	27.2	0.425	0	6 mos.	None	820 Gm.	Sarcoma	.....	.....	Died 5/23/35; autopsy; radiotherapy helped for a time; sarcoma of spleen
40	64	♂	3/ 3/32	64	3.1	3,200	44	10.2	0.45	0	2 yrs.	None	Palpable	.....	.....	.....	Died 7/5/32; apparently cerebral accident; diagnosis unknown
41	21	♂	4/ 5/33	108	6.1	15,700	74	4.6	0.50	0	4 yrs.	None	3 cm. below costal margin	.....	.....	.....	No change, 1/8/35; diagnosis unknown

* All patients had anemia (except patient 41) and all were jaundiced.

2. Haden, R. L.: Am. J. M. Sc. **188**: 441 (Oct.) 1934.

3. Thompson, W. P.: Bull. Johns Hopkins Hosp. **42**: 113 (March) 1928.

4. Rich, A. R., and Rienhoff, W. F.: Bull. Johns Hopkins Hosp. **36**: 431 (June) 1925.

of splenectomy. Our therapeutic results in the eighteen cases in which spenectomy was performed are uniform and coincide with the results of others. Removal of the spleen is immediately followed by cessation of the increased hemolytic activity. Relief is immediate and, apparently, permanent.

A study of the factors that might be influenced by splenectomy results in the acceptance of only one; the excessive hemolysis stops. I can see no reason to consider any other influence, as the cessation of excessive hemolysis will explain all the changes observed.

With the removal of the site of increased destruction of erythrocytes, the serum bilirubin and the urobilin excretion figures drop promptly to normal levels. The already overactive bone marrow rapidly raises the erythrocyte concentration in the peripheral blood. As the red blood cell count rises, the stimulus for new erythrocytes falls and the proportion of reticulocytes drops. All these changes toward normal appear within a few hours after operation and are concluded in from two to three weeks. We have yet to observe any changes suggesting subsequent increase above normal in erythrocyte destruction. The results of operating appear to be permanent.

The only other theoretically possible effect of splenectomy would be some change in the spherical cells and their fragility. That some such change does occur has been suggested at various times by various authors. Their conclusions are, as a rule, variable, and the changes usually observed are slight shifts in the fragility test.

Our observations warrant the definite conclusions, in the postsplenectomy cases, that the spherical cells persist with their attendant fragility changes for as long after splenectomy as time has permitted observation. The proportion of these typical cells may vary within relatively narrow limits, but they have been demonstrated in patients sixteen years after operation in concentrations as high as 14 per cent.

The recent report of Lord Dawson of Penn[5] of typical fragility changes persisting forty-five years after splenectomy leaves little doubt that the spherical cells are not affected by this surgical procedure.

TABLE 4.—*Relation of Red Cell Diameter and Fragility to Hypotonic Salt (Vallery-Radot)*

	Diameter of Red Blood Cells in Microns	Hemolysis Begins, per Cent NaCl
Man	7.6	0.42
Guinea-pig	7.5	0.44
Monkey	7.2	0.44
Dog	6.6	0.50
Rabbit	6.3	0.52
Horse	6.2	0.54
Rat	6.0	0.54
Cat	5.6	0.60
Goat	5.3	0.72

What may be termed the life history of this disease can best be presented by a brief review of the records of two of our patients:

These patients are half sisters. Their father, for many years before his death, suffered from chronic anemia and jaundice, as did the grandfather. A diagnosis of hemolytic jaundice was never made but it seems more than likely that they had this disease.

Our two patients had a normal, healthy childhood. In 1898 both became chronically ill with a sallow color and anemia. Many physicians were consulted, various diagnoses were offered, a multitude of medicinal preparations was prescribed and taken but the chronic anemia and jaundice continued.

In 1920, after twenty-two years of this chronic intermittent disorder, the younger sister came to the Presbyterian Hospital because of a recent attack of colic in the right upper quadrant. A diagnosis of cholelithiasis was made and operation advised. April 10 a gallbladder containing stones was removed. At the same time the spleen was taken out. Convalescence was stormy but the patient survived. Histologic study on sections of the spleen is recorded as being compatible with hemolytic jaundice —the patient's clinical diagnosis is recorded at the time she left the hospital as chronic cholelithiasis and splenic anemia. She then disappeared from medical observation, the disappearance being due not only to the fact that no further attacks of colic were experienced but also because the chronic jaundice vanished.

TABLE 5.—*Respective Blood Studies in Half Sisters*

	F. L.	A. L.
Red blood cells	5,000,000	3,000,000
Hemoglobin	104% (Sahli)	70% (Sahli)
White blood cells	9,600	6,900
Polymorphonuclears	53%	76%
Reticulocytes	1.1%	20.4%
Microcytes	13%	20%
Fragility	0.475% NaCl	0.525% NaCl
Serum bilirubin	Very faint trace	3.6 mg. per 100 cc.

Fifteen years later we were reviewing the sections of spleen collected by the Department of Surgical Pathology. Although the sections were old and faded, one glance at the spleen of this patient warranted the diagnosis of typical hemolytic jaundice. The patient and her sister were pursued and their clinical pictures brought up to date.

There is no question that both these patients have typical hemolytic jaundice. Spherical microcytes are present in the peripheral blood of both, and the response of their blood to hypotonic salt solutions is similar and typical. In one, splenectomy resulted in a cessation of excessive erythrocyte destruction. In the other this excessive destruction with its attendant jaundice and anemia continues now into its thirty-eighth consecutive year. Their respective blood studies at the present time are given in table 5.

It would seem that there was little doubt but that these two patients inherited the spherical microcytes from their father. The hemolytic jaundice became active in the two at approximately the same time and continued in one until splenectomy twenty-two years later and in the other to the present time, thirty-eight years after the onset.

The blood of the two patients contains spherical microcytes in approximately the same proportions. As far as one can see, the only difference between these two patients is the spleen. In one the active phase of the disease ceased with splenectomy sixteen years ago; in the other the active phase continues.

This evidence, I feel, warrants the conclusions that, given the inherited spherical microcytes and increased hemolytic activity, one has the disease known as typical hemolytic jaundice and that this disease, once active, remains active until the site of increased hemolytic activity is removed.

Three important unsolved questions remain:

1. Little or nothing is known about the genetics of transmission of these spherical cells.

2. Little or nothing is known about the factors that initiate the excessive hemolysis which signals the onset of the active disease. It is known that individuals exist, as members of hemolytic jaundice families, whose blood contains these spherical cells and in whom increased hemolysis is not taking place. We also know that these latent cases may become active at any time in their career from, in our series, the age of 6 weeks to the age of 58 years. We also know that, when the disease once becomes active, spontaneous remission will not occur and that chronic anemia with jaundice will

5. Dawson, B. E.: Brit. M. J. 2: 699 (Oct. 15) 1932.

persist until splenectomy. But we have not been able to associate the change from latency to activity with any as yet discernible event. Occasionally an acute infection precedes the onset of jaundice; in the majority of cases no such history can be elicited.

3. We do not know whether a normal spleen interposed in a circulation containing spherical erythrocytes would behave as and assume the histologic characteristics of a spleen presenting hemolytic jaundice.

CONCLUSIONS

1. Hemolytic anemia with jaundice and splenomegaly has been observed in forty-five patients.

2. This syndrome may be separated into two groups:

(*a*) Typical hemolytic jaundice.
(*b*) Atypical hemolytic anemia.

3. Typical hemolytic jaundice is a clear cut definite disease entity the course of which can be predicted and the mechanism of which is beginning to be understood.

4. The atypical hemolytic anemias comprise a heterogeneous group of conditions in which there is increased red cell destruction.

5. The symptoms of typical hemolytic jaundice are promptly, completely and permanently relieved by splenectomy. The atypical hemolytic anemias have not been benefited by this procedure.

6. Accurate preoperative diagnosis is of great importance.

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THE RESULTS OF SPLENECTOMY IN THROMBOCYTOPENIC PURPURA

A COMPARATIVE STUDY OF TEN CASES IN WHICH SPLENECTOMY WAS PERFORMED AND ELEVEN CASES TREATED BY CONSERVATIVE METHODS

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Two centuries have elapsed since Werlhof originally described a case of purpura haemorrhagica, but the advances made in our knowledge of the disease have all occurred in the past fifty years. Its clinical manifestations remain as he so vividly described them, though little is known, even today, about the mechanism of their production. Its characteristic blood picture has become familiar. It is well known that many cases are closely associated with the factor of infection, that some are caused by toxic agents and that others occur in the course of diseases affecting the hematopoietic and reticulo-endothelial systems. Some of these cases can be treated effectively. There is, however, a group of cases in which the etiology remains entirely obscure. Strangely enough, it is this group that can be treated with the greatest assurance of success.

For many centuries, physicians have recognized the existence of hemorrhagic diseases. It was not until 200 years ago, however, that purpura haemorrhagica emerged from this group as a clinical entity. The disease was first described in 1735 by one of the greatest physicians of the eighteenth century, Paul Gottlieb Werlhof.[1] During the following century and a half no important contribution was made to the knowledge of the disease, and it remained in comparative obscurity. In 1887 an observation of great importance was made by Denys,[2] a Belgian histologist. He pointed out an almost complete absence of platelets in blood smears of some patients with purpura. Two years later Hayem [3] called attention to this finding and in 1891 [4] reported two cases of purpura presenting low platelets and poor clot retractility—the latter being an observation which was apparently original with him. Four years later he [5] wrote "The two constant and pathognomonic characteristics are the rarity of hematoblasts and the absence of transudation of serum after the coagulation of the blood" (les deux caractères constants et pathognomoniques sont donc la rareté des hématoblastes et l'absence de transsudation du sérum après la coagulation du sang). In 1909 Pagniez [6] demonstrated a connection between clot retraction and the number of platelets, and in the following year Duke [7] described the method still in use for the estimation of bleeding time and reported two cases of purpura in which the bleeding time was prolonged. The next landmark in the history of the disease came in 1916 when, at Kaznelson's suggestion,[8] Professor Schloffer of Prague performed the first splenectomy in a case of purpura haemorrhagica. The dramatic results of this operation were reported in the same year by Kaznelson.[9] This report stimulated renewed interest in purpura and much has been written on the subject since. The results of splenectomy have received considerable attention and the operation, though still resting on an empirical basis, has become firmly entrenched as the most effective form of therapy in certain cases.

Since Kaznelson's paper in 1916, many excellent reports on the results of splenectomy in thrombocytopenic purpura have come from European and American clinics. In 1926 Whipple [10] reviewed eighty-one cases, including three of his own. The operative mortality in this group was 16 per cent. Two years later Spence [11] was able to add twenty-three more cases,[12] bringing the total number of reports published in the two groups to 104. In the following year Quénu [13] collected a number of additional cases and found an operative mortality of 16 per cent for the entire series of 122 cases. In 1932 Eliason [14] summarized the situation to date, giving

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Owing to lack of space, this article has been abbreviated for publication in THE JOURNAL by the omission of a number of case reports. The complete article appears in the authors' reprints.

1. Werlhof, P. G.: Opera Medica (collegit et auxit, J. E. Wichmann, Hanover, 1775); Excerpta e Commercio Norico, 1731-1745, p. 748. The disease is still referred to frequently, especially on the continent, as morbus maculosus Werlhofii.

2. Denys, J.: Etudes sur la coagulation du sang, Cellule **3**: 445, 1887. The priority of this observation has been contested by Minkowski, who stated that it was made by Brohm in 1883.

3. Hayem, G.: Du sang et de ses altérations anatomiques, Paris, 1889, p. 970.

4. Hayem, G.: Sur un cas de diathèse hémorrhagique, Bull. et mém. Soc. méd. d. hôp. de Paris **8**: 389-394 (July 17) 1891.

5. Hayem, G.: Du purpura, Presse méd. **3**: 234, 1895.

6. Pagniez, P.: Aperçu sur l'état actuel de la question des plaquettes sanguines, Arch. d. mal. du coeur **2**: 18, 1909.

7. Duke, W. W.: The Relation of Blood Platelets to Hemorrhagic Disease, J. A. M. A. **55**: 1185 (Oct. 1) 1910.

8. Whipple [10] called attention to a personal communication from Dr. E. W. Peterson informing him that splenectomy was suggested for a case of purpura in 1915 by Dr. Alfred Hess of New York.

9. Kaznelson, P.: Verschwinden der hämorrhagischen Diathese bei einem Falle von "essentieller Thrombopenie" (Frank) nach Milzexstirpation: Splenogene thrombolytische Purpura, Wien. klin. Wchnschr. **29**: 1451-1454 (Nov.) 1916.

10. Whipple, A. O.: Splenectomy as a Therapeutic Measure in Thrombocytopenic Purpura Haemorrhagica, Surg., Gynec. & Obst. **42**: 329-341 (March) 1926.

11. Spence, A. W.: The Results of Splenectomy for Purpura Haemorrhagica, Brit. J. Surg. **15**: 466-499 (Jan.) 1928.

12. Spence included reports of 101 cases in his series. However, he did not include four of Whipple's cases and, as pointed out by Eliason, Farley's patient was the same as Lee's. Therefore, he actually added twenty-three new cases to the eighty-one collected by Whipple.

13. Quénu, J.: Les résultats de la splénectomie dans le purpura hémorragique, Rev. de chir. **67**: 24-39, 1929.

14. Eliason, E. L., and Ferguson, L. K.: Splenectomy in Purpura Haemorrhagica, Ann. Surg. **96**: 801-829 (Nov.) 1932.

figures on 213 collected cases, five of which were his own. The results of splenectomy in this group were excellent. Cures were reported in 73 per cent and improvement in an additional 8 per cent; i. e., 81 per cent of the patients were benefited by the operation. The operative mortality was 13 per cent for the entire group but only 7 per cent in the 113 cases reported between 1928 and 1932. Of the 156 cases reported as cured, only five had been followed for five or more years. In the same year Giffin [15] published the results in forty-four cases in which splenectomy was done at the Mayo Clinic. The operative mortality was 7 per cent. However, twenty splenectomies were performed for purpura between March 7, 1923, and Jan. 1, 1927, without a single operative mortality. One patient died of a recurrence of the disease five years after operation. The remaining nineteen patients were alive and had suffered no serious hemorrhagic manifestations in a follow-up period of from five to nine years. In 1934 Pemberton [16] reported thirteen more cases from the Mayo Clinic, bringing their total to fifty-seven cases, the largest series so far published from any single clinic. Four patients died while still in the hospital, giving a figure for operative mortality of 7 per cent for the whole group, or the same as that quoted by Giffin for their first forty-four cases. Permanent remission of the disease was achieved in 63 per cent of the patients who survived; an additional 35 per cent were improved, and in only one case did the disease recur in acute form.

Ever since the introduction of splenectomy in the treatment of thrombocytopenic purpura, surgeons have attempted to divide the disease into acute and chronic types. This has resulted in considerable confusion, as many of them have not defined the terms "acute" and "chronic." It is apparent that some surgeons include all fulminating cases in their acute group, regardless of the duration of the disease, thus including chronic cases in acute exacerbations. This has naturally led to inaccuracies in the results published for both groups. Nevertheless, it is only fair to point out that, if anything, this would tend to decrease the mortality for the chronic group without materially affecting the mortality for the acute group.

Until comparatively recently it was felt by most surgeons that splenectomy was definitely contraindicated in acute cases. Whipple (1926) reported seven deaths in eight cases of acute purpura, and Spence (1928) found ten deaths in twelve cases. Eliason (1932) gave an operative mortality of 34.3 per cent for the thirty-five acute cases in his series but called attention to a drop to 13.6 per cent in the twenty-two splenectomized between 1928 and 1932. At present the available figures indicate an operative mortality of about 7 per cent for all cases of thrombocytopenic purpura, that for the acute cases being in the vicinity of from 13 to 14 per cent and for the chronic cases from 5 to 6 per cent.

It is apparent from these figures that factors have come into play in recent years which have strikingly reduced the mortality from splenectomy. These factors are probably:

1. More accurate diagnosis.
2. Better preoperative preparation of the patient.
3. Advances in surgical technic and a more careful choice of the anesthetic.

15. Giffin, H. Z.: Problems Associated with the Treatment of Essential Thrombocytopenic Purpura: Notes on Forty-Four Cases in Which Splenectomy Was Performed, Tr. A. Am. Physicians **47**: 218-227, 1932.
16. Pemberton, J. deJ.: The Diagnosis and Treatment of Purpura Haemorrhagica, Am. J. Surg. **24**: 793-806 (June) 1934.

The operative mortality will probably always be higher in fulminating cases, irrespective of the duration of the disease, since the patients are in a more serious condition when they come to operation. It also seems likely that it will always be higher in the incipient group, as correct diagnosis is often impossible in these cases, the purpura and thrombocytopenia frequently being merely manifestations of some underlying disease which only subsequent events will reveal in its true colors. It is, however, no longer so high that it can be considered a contraindication to a measure which, when performed by an experienced surgeon in selected cases carefully prepared for operation, may be the means of saving life.

MATERIAL

It is our purpose in this paper to present twenty-one cases of so-called idiopathic thrombocytopenic purpura studied in this clinic in the past sixteen years.[17] This group includes all cases adequately enough worked up and sufficiently followed to establish the diagnosis beyond reasonable question. In ten of these patients splenectomy has been done. They have been followed for an average period of five and one-half years, (five of them for over six years)—the longest follow up being eleven years and the shortest eleven months. The eleven nonsurgical cases are presented as a control group. They have been followed for an average period of four years (six of them for over three and a half years)—the longest follow up being eleven years and the shortest one month. We have appended the reports of two cases not included in this group to illustrate the criteria used in the selection of cases.

REPORT OF CASES

CASE 1.—*History.*—A. V. V., an American born schoolboy, aged 12 years, was admitted to the hospital in July 1920 for purpura of the skin, epistaxis and bleeding gums of four days' duration. The family history showed no "bleeders." The past history was essentially negative. The diet was adequate in every respect. On physical examination the boy was healthy looking, with skin speckled with fine purpuric spots and ecchymotic areas. The eyes and ears were normal. The nose contained dry crusts of blood. The condition of the teeth was fair; the gums were oozing. The tonsils were large and cryptic but apparently not infected. There were moderately enlarged lymph glands in both axillae but nowhere else. The spleen was not palpable, and there were no other significant changes.

Laboratory Examination.—Examination of the blood revealed: red blood cells 3,200,000, hemoglobin not recorded, white blood cells 12,200 with a normal differential count, bleeding time 5 minutes, clotting time 25 minutes, clot retraction prolonged, platelets not counted. The urine showed many red blood cells; a stool guaiac test for occult blood was strongly positive.

Course.—About one week after admission the patient was given a transfusion of 350 cc. of citrated blood. Following this he seemed definitely better and all bleeding stopped; red blood cells rose to 4,100,000 with a hemoglobin of 84 per cent (Sahli), bleeding time dropped to 2 minutes, clotting time to 6 minutes, the clot retracted normally and no more blood was found in the urine or stool. The patient was discharged after two weeks in the hospital and for the next eight months was followed closely in the clinic. A month after discharge, mild purpuric symptoms recurred and persisted for a short time. He then passed through a period of several months when he was free from all bleeding but in March 1921 had to be readmitted with a fairly severe recurrence.

On this admission the physical examination was essentially as reported previously except that his teeth had been cleaned up and were in excellent condition. The red and white cell counts and the hemoglobin were all within normal limits; the platelets were 20,000. He was tried out on an emulsion of turpentine

17. Because of lack of space this paper is abbreviated in THE JOURNAL by the inclusion of reports of only six cases. The entire series will be found in the authors' reprints.

and acacia (10 minims [0.6 cc.] three times a day) and also received four transfusions, to which he was slow in responding. After two months he was discharged with all bleeding stopped, but the platelets numbered only 5,000. For the next three and one-half years his course, as followed in the outpatient department, was relatively benign and, though the platelet count never rose over 95,000, he remained practically free from bleeding. In October 1924, however, he again had an acute flare up requiring admission.

On this occasion the platelets numbered 20,000, bleeding time 31½ minutes, clotting time 7 minutes. He remained in the hospital eight weeks and showed slow but steady improvement. After leaving the hospital he failed to maintain his improvement and was readmitted for splenectomy three weeks after discharge. At this time, however, his bleeding was minimal; the platelets were too few to count accurately. Operation was performed by Dr. Allen O. Whipple on December 27, being preceded by a transfusion of whole blood. The postoperative course was uneventful. Platelets rose abruptly on the third day after operation to 180,000; bleeding time dropped to 2 minutes and all gross bleeding ceased. The platelet rise, however, was not maintained, and, though the patient had no further symptoms save an occasional purpuric spot on the skin, the count on discharge, three weeks later, had dropped back to 10,000.

For a time it seemed as though the disease had been permanently arrested, for the patient was free from all bleeding for the next eight months. Toward the end of the first year after operation, however, he had two colds and broke out with mild bleeding manifestations with each. The platelet count never went above 80,000, and eighteen months after splenectomy he was admitted for the fifth time in a fulminating flare up of the disease. Despite two transfusions and the administration of blood coagulants, he died of a cerebral hemorrhage four days after admission. Permission for a postmortem examination, unfortunately, could not be obtained.

Summary.—A case of severe chronic thrombocytopenic purpura in an adolescent boy was followed through its entire duration of six years. Splenectomy was performed during a relatively quiescent phase of the disease without material benefit. The most outstanding characteristic of the case was its susceptibility to severe exacerbations, of which there were four, the last ending fatally.

CASE 5.—*History.*—M. M., a Russian-Jewish schoolboy, aged 13 years, first admitted to this hospital in August 1928, gave an eight year history of frequent epistaxis and easy bruising. There were no "bleeders" in his family and the past history was essentially negative. On physical examination he appeared chronically ill but aside from petechiae, ecchymosis, a spleen that was felt with difficulty, and a positive tourniquet test there were no other significant physical changes. A laboratory work up showed: hemoglobin 65 per cent; red blood cells 3,700,000; white blood cells 8,700, with a normal differential count; platelets 6,000; bleeding time 10 minutes; clotting time 3 minutes; clot retraction poor; urine negative for red blood cells; stool guaiac test strongly positive. After a thorough search for foci of infection had been made with negative results it was decided that he had "idiopathic" thrombocytopenic purpura and that the spleen should be removed.

Course.—August 20 a splenectomy, followed by transfusion, was performed by Dr. F. B. St. John. Following operation his course was very smooth and he had a splendid platelet rise. On the third postoperative day the platelets were 210,000 and on the ninth postoperative day they were 360,000. By his sixteenth day the bleeding time had fallen to 1½ minutes and since then the platelets have never been below 175,000 nor his bleeding time above the figure just given. Interestingly enough, though the bleeding time has always been within normal limits, the clot retraction has remained prolonged. He is recorded to have had a slight epistaxis about six weeks after splenectomy and another twenty months later, but there have been no other episodes of bleeding. A noteworthy feature of this case was the patient's leukocyte response to what appears to have been an acute pharyngitis and tonsillitis, which occurred three weeks after operation. This response consisted of a marked lymphocytosis, reaching as high as 81 per cent in a total white cell count of 21,000. A relative lymphocytosis was reported as late as May 1930, but there has been no reason to believe that the patient has a lymphatic leukemia. He was last seen in the Spleen Clinic in February 1936 and at that time was in perfect health with no clinical evidence or history of bleeding. The blood values were all well within normal limits, with the exception of the clot retraction, which was still prolonged; the capillary resistance, as measured by the Dalldorf apparatus, was 40.

Summary.—In a case of moderately severe chronic thrombocytopenic purpura a seven and one-half year follow up has revealed no convincing evidence of a recurrence of the disease following splenectomy—a dramatic result thus far.

CASE 9.—*History.*—G. S., an American-born schoolgirl, aged 15, admitted to the hospital in April 1933, complained of easy bruising and profuse epistaxis for the previous seven years and vaginal bleeding for the previous six months. Her mother had pernicious anemia, which was being controlled with liver therapy. The patient had always eaten a well balanced diet. She was said to have had rheumatic fever and chorea eight years previously. The bleeding tendency had started following a tonsillectomy and had subsequently become sufficiently severe to require five admissions to another hospital. All efforts at conservative therapy (including repeated transfusions and a course of x-ray treatments to the spleen) had failed to alter the course of the disease more than temporarily. On physical examination the patient was markedly exsanguinated with extreme pallor, rapid, thready pulse and cold extremities. The skin was clear. The eyes, ears, nose and throat were all normal. The teeth were all excellent. The spleen was not palpable. There was profuse bleeding from the vagina. The remainder of the examination was not noteworthy.

Blood Studies.—Hemoglobin was 32 per cent, red blood cells 2,200,000, white blood cells 5,700, with a normal differential count, platelets 15,000, bleeding time 4 minutes, clotting time 5½ minutes and clot retraction not reported.

Course.—Immediate operation was deemed advisable and the patient's spleen was removed by Dr. Allen O. Whipple on the day following admission. During the operative procedure the patient had a sudden, very profuse epistaxis which made it seem doubtful at the time whether she would leave the operating table alive. Her condition, however, was improved markedly by transfusion and other supportive measures and by the second postoperative day the platelets had risen to 356,000. On the third day after operation all bleeding ceased, and on the sixth day the platelets spiked to a high of 1,025,000, but during the next ten days they dropped back to 111,000. She left the hospital three weeks after operation, having had a smooth postoperative course, and on discharge the hemoglobin was 70 per cent, red blood cells 4,100,000, platelets 134,000. During her subsequent follow up she has had no recurrence of purpuric manifestations and the platelets have remained at or above 129,000. She has recently had two nosebleeds, however, which, in the opinion of a consulting otolaryngologist, are a purely local phenomenon and are not connected with the patient's general condition. The most recent bleeding time was 2½ minutes.

Summary.—In a case of severe chronic thrombocytopenic purpura, splenectomy was performed as a life-saving measure during an exsanguinating exacerbation of the bleeding tendency. As far as one can judge from a two and one-half year follow up, the disease is cured.

CASE 13.—*History.*—R. V., a Russian-Jewish housewife, aged 40, admitted to the hospital May 5, 1921, complained of bleeding from the vagina, nose and gums and into the skin for the previous three months. There were no bleeders in the family. The patient had always been healthy until the onset of her illness. Her periods had been regular and not excessive until three months prior to admission, when she began to have menorrhagia. Her last period had started eighteen days previous to entering the hospital and she was still bleeding profusely on admission. On examination the patient was obviously anemic and very weak. Scattered over the trunk and extremities were many old and new purpuric spots of various sizes. Two retinal hemorrhages were present in the left eye. The ears and throat were normal. The nose contained several crusts of dried blood. The teeth were in poor condition and the gums were oozing freely. The spleen was not felt. The patient was bleeding profusely from the vagina. There were no other abnormal changes.

Laboratory Examination.—Hemoglobin was 28 per cent (Sahli), red blood cells, 2,700,000, white blood cells, 17,500 with

polymorphonuclears 79 per cent, platelets too few to count, bleeding time 36 minutes, clotting time 5 minutes. The urine contained many red blood cells; stool guaiac test was negative.

Course.—The patient was given an immediate transfusion of citrated blood and the vagina was packed tightly. For the first month she continued to bleed profusely from the uterus despite packing and eight transfusions. Her teeth were attended to, and various forms of therapy were tried, such as intracutaneous injections of old tuberculin and oral administrations of turpentine, but the bleeding, particularly from the vagina, continued unabated. Finally, radium was applied to the interior of the uterus to produce an artificial menopause, and shortly thereafter all vaginal hemorrhage stopped. The patient received two more transfusions, making ten in all, but within a short period of time many bilateral retinal hemorrhages developed, producing partial blindness. Toward the end of the second month, however, the bleeding manifestations became milder and the platelet count finally rose to 30,000. She was discharged three and one-half months after admission, apparently free from bleeding, with normal red and white counts, normal hemoglobin and a platelet count of about 70,000. Unfortunately the patient returned immediately to her home in Texas. In 1932 (eleven years later) she reported by letter that she had completely recovered her vision and that she had been in perfect health since leaving the hospital, except for occasional purpuric spots on the skin.

Summary.—A case of severe incipient thrombocytopenic purpura in a middle aged woman, characterized at the onset by intractable uterine bleeding, was apparently controlled by radium sterilization. The disease has since become mild and chronic. The total follow up has been eleven years.

CASE 15.—*History.*—M. G., an Irish-American schoolgirl, aged 11 years, admitted to the hospital March 10, 1929, complained of a brown skin rash and bleeding from the mouth and nose of three weeks' duration. The mother and a paternal aunt bruised easily; otherwise there was no history of bleeding in the family. Tonsillectomy had been done seven years before. For the previous six months the mother had noted that the patient bruised easily. Present illness: In addition to the sudden onset of skin rash, epistaxis and bleeding gums, the child had been nauseated on several occasions within the previous three weeks, and her appetite was failing. On examination the patient was well nourished and well developed and did not appear ill. There were numerous small purpuric spots scattered over the entire body, with several large ecchymotic areas on both lower extremities. The eyes and ears were normal. The nose showed evidence of recent epistaxis. The teeth were excellent, the tonsils were out and the throat was entirely normal. The spleen was not palpable. Examination was otherwise negative except for slight enlargement of cervical lymph nodes and a positive tourniquet test.

Laboratory Examination.—Hemoglobin was 70 per cent, red blood cells 3,400,000, white blood cells 9,500 with a normal differential count, platelets 35,000, bleeding time 28½ minutes on one occasion and over an hour on another. Clotting time was 3 minutes, clot retraction was normal once and "fair" a second time. Roentgenograms of the sinuses were negative. The urine contained a few red blood cells.

Course.—The child was observed in the hospital for three weeks and received one small transfusion just before discharge. The platelets hovered between 35,000 and 40,000, and she continued to have mild bleeding manifestations throughout her stay. Splenectomy was considered, but her symptoms were not deemed severe enough to warrant operation, and she was discharged to the care of her local physician to be readmitted for immediate operation if the disease showed any increase in severity. Two days after discharge she began to bleed profusely from the gums and urinary tract. These symptoms persisted and three days later a slight speech difficulty was noted. The seventh day after leaving the hospital she began vomiting blood, became stuporous and was rushed back to the hospital, where she died forty minutes after admission from obvious cerebral hemorrhage. At necropsy, massive subdural, subarachnoid and cerebellar hemorrhages, both old and new, were found. In addition, extravasations of blood were found in the majority of the abdominal organs. There were no other significant changes.

Summary.—A deceptive, moderately severe incipient case of thrombocytopenic purpura occurred in an 11 year old child. The disease suddenly became fulminating and terminated fatally seven months after onset. This case illustrates how treacherous the disease can be.

CASE 20.—*History.*—B. S., a Russian-Jewish housewife, aged 51, first seen in the outpatient department Jan. 1, 1933, gave a history of intermittent bleeding into the skin and from the nose since the age of 12, and of profuse menorrhagia since the onset of the menses. She had had fairly severe postpartum hemorrhages after three deliveries. In addition, she stated that she had gone through an episode of headache, syncope and transient blindness in the left eye accompanied by hematemesis and melena one and one-half years previously. Two years prior to being seen in the clinic, splenectomy had been offered by another hospital. Operation was refused and high voltage roentgen therapy to the spleen had been substituted in its stead. The latter had resulted in a mild exacerbation of the bleeding tendency and the onset of an artificial menopause. There was no history of blood dyscrasia in the family. On examination the patient was obese, and did not appear ill. Her skin was speckled with a fine purpuric rash, and several large areas of subcutaneous ecchymosis were also noted. The ears, nose and throat were negative. The teeth were considered only "fair." The remainder of the physical examination was irrelevant. The spleen was not felt.

Laboratory Examination.—The blood readings were as follows: Hemoglobin 88 per cent, red blood cells 5,400,000, white blood cells 6,900, polymorphonuclears 72 per cent, platelets 8,000, bleeding time 4½ minutes, clotting time 2¼ minutes, tourniquet test positive.

Course.—The patient refused to consider splenectomy and also refused to enter the hospital for observation and transfusion. She was followed closely in the hematology clinic for a period of about six months and was then lost sight of for a year and a half. During the latter period she had a hemorrhage into the right eye, which cleared up uneventfully. On her last visit, in February 1935, she was improved and the platelets numbered 18,000, the highest they had ever been while she was under observation in this clinic. The bleeding time on this and on one prior occasion was slightly over 10 minutes.

Summary.—A case of moderately severe chronic thrombocytopenic purpura of over forty years' duration was followed in this clinic for a period of twenty-four months and then lost sight of. Splenectomy was obviously indicated but repeatedly refused. Interesting features of the case were its extremely long duration and the fact that, though on at least two occasions the disease became severe enough to produce ocular and cerebral symptoms, there were no permanent residua.

The cases all belong to the group of thrombocytopenic purpuras commonly referred to as "idiopathic" or "essential."[18] They have been selected because in no instance was an obvious causative factor involved and in no instance did the purpura occur in the course of some other disease affecting the hematopoietic or reticulo-endothelial systems. As far as possible we have excluded all cases in which an associated infection might reasonably be considered responsible for the purpura. The exaction of such a rigid standard in the choice of material has naturally resulted in the omission of several cases that would ordinarily be considered acceptable in this group (i. e., cases 11 and 12). We believe, however, that a fairer appraisal of the results of treatment can be made when such a standard is adhered to.

In classifying our cases we have followed the outline proposed by Giffin in 1932. This divides the group into (1) chronic cases and (2) incipient cases in their primary attack, irrespective of the exact duration of the disease. The cases have been further subdivided by characterizing them as mild, moderate or severe.

18. We feel very strongly that these terms should be discarded, as it is misleading to imply the absence of a causative factor merely because one is ignorant of its nature.

AGE AT ONSET, SEX, NATIONALITY AND RACE

Of the twenty-one cases here presented in the control and operative groups 76.2 per cent, or slightly more than three fourths, became manifest before the fourth decade. There were seven in the first decade, five in the second, four in the third, two in the fourth and three in the fifth. The disease was more than four times as prevalent among females as among males, the exact ratio of distribution between the sexes being seventeen to four. In this connection it is of interest to note that six of the seven patients in whom the onset took place during the first decade were females. This finding is noteworthy in that in their paper on purpura in childhood, McLean, Kreidel and Caffey [19] found that the males outnumbered the females by two to one. As far as the nationality is concerned, our observations are in agreement with those of other observers in that the disease showed no predilection for race or nationality: the two series embraced four Americans, one American Negress, four Italians, one Austrian, two Irish, one Irish-American, one Swedish-American, and seven of Russian-Jewish extraction. The high incidence of the last mentioned may be partially explained, we think, by the fact that the Presbyterian Hospital is located in a district in which the population is largely Jewish.

TABLE 1.—*Initial Blood Picture and Severity on Admission in Group in Which Operation Was Performed*

Case	Severity	Platelets	Bleeding Time	Clotting Time	Clot Retraction	Tourniquet Test	Hemoglobin (% Sahli)	Red Blood Cells in Millions	White Blood Cells in Thousands	Polymorphonuclears	Lymphocytes	Other Cells*
1	Moderate	Not counted†	5′ ‡	25′ ‡	Prolonged	Not done	Not done	3.2	12.2	55	27	18
2	Moderate	Too few to count	9′	8′	Prolonged	Not done	75	4.1	10.3	59	24	17
3	Mild	15,000	3′30″	4′	Normal	Not done	53	3.3	10.9	74	23	3
4	Severe	28,000§	58′	1′30″	Not done	Not done	21	1.9	24.0	84	10	6
5	Moderate	6,000	10′	3′	Prolonged	Positive	65	3.7	8.7	60	32	8
6	Moderate	15,000	5′30″	3′	Prolonged	Not done	56	3.1	9.9	73	21	6
7	Severe	6,000	7′	5′	Not done	Not done	33	3.2	5.5	85	10	5
8	Moderate	19,000	15′ plus	5′	Prolonged	Positive	75	5.3	8.6	52	32	16
9	Severe	15,000	4′	5′30″	Not done	Not done	32	2.2	5.7	65	25	10
10	Moderate	26,000	15′30″	2′45″	Prolonged	Positive	75	3.8	6.9	72	16	12

* Eosinophils, basophils and monocytes.
† 20,000 8 months later at his second admission (prior to operation).
‡ Accuracy of these values open to question.
§ Interns count; no platelets seen in admission blood smear.

TABLE 2.—*Initial Blood Picture and Severity on Admission in Group in Which Operation Was Not Performed*

Case	Severity	Platelets	Bleeding Time	Clotting Time	Clot Retraction	Tourniquet Test	Hemoglobin (% Sahli)	Red Blood Cells in Millions	White Blood Cells in Thousands	Polymorphonuclears	Lymphocytes	Other Cells
13	Severe	Too few to count	36′	5′	Prolonged	Not done	28	2.7	17.5	79	19	2
14	Moderate	15,000	21′20″	2′30″	Prolonged	Positive	74	4.1	8.6	54	37	9
15	Moderate	35,000	28′30″	3′	"Fair"	Positive	70	3.4	9.5	59	36	5
16	Mild	45,000	15′	1′	Prolonged	Positive	100	5.8	5.5	48	50	2
17	Mild	20,000	4′30″	5′30″	Normal	Negative	45	3.1	10.0	73	19	8
18	Moderate	8,000	33′ plus	3′	Prolonged	Not done	78	4.4	10.5	66	22	12
19	Mild	28,000	9′45″	3′	Prolonged	Faintly positive	85	3.9	8.4	78	14	8
20	Moderate	8,000	4′30″	2′15″	Not done	Positive	88	5.4	6.9	72	16	12
21	Moderate	6,000	12′	2′30″	Not done	Not done	63	3.9	5.8	60	26	14
22	Moderate	12,000	6′30″	2′30″	Prolonged	Not done	75	3.2	7.2	47	48	5
23	Mild	40,000	3′50″	5′45″	Prolonged	Not done	76	4.4	5.3	65	34	1

TYPE OF DISEASE

Fifteen of the cases were chronic and six were incipient. Of the former, five were mild, seven moderately severe and three severe. Of the latter, none were mild, five were moderately severe, and one was severe.

CLINICAL PICTURE

The clinical picture here recorded appears as it was noted by the examiner on the patient's first admission to the hospital or first observation in the outpatient department. Skin purpura was present in all but two cases on the first examination. Bleeding into or from the mucous membranes was present in eleven instances. Gross or microscopic hematuria was recorded in only six cases. In only one was there frank bleeding from the bowel. In four others the guaiac test of the stool was reported as positive, but in three of these it could have been due to swallowed blood. Retinal hemorrhages were noted in two cases and vitreous hemorrhage was noted in one. In eight of the twenty-one cases the spleen was recorded as palpable on the initial examination; one of these cases was incipient, the disease having been present according to the history for four days; the remaining seven were chronic. Thus the spleen was palpable in one out of five incipient cases and in seven out of fifteen chronic cases.

BLOOD PICTURE

From tables 1 and 2 it will be seen that the initial blood observations in our two groups of cases conform closely to the hematologic diagnostic criteria which have come to be associated with so-called idiopathic thrombocytopenic purpura. In none of the twenty-one cases did the platelet count exceed 45,000. The bleeding times were for the most part prolonged, and the clotting times were generally normal. The clot retraction was delayed in thirteen cases, not done in five, normal in two, and recorded as "fair" in one. The tourniquet test was reported in nine cases: in seven of these it was positive, in one faintly positive, and in one negative. The values for red blood cell count and hemoglobin varied from a low of 1,900,000 with 21 per cent hemoglobin to 5,800,000 with 100 per cent hemoglobin. In those cases in which anemia was present it was of the secondary type and varied with the duration, degree and extent of clinical bleeding. No white counts below 5,300 were recorded and the highest figure was 24,000.

19. McLean, Stafford; Kreidel, Katherine, and Caffey, John: Hemorrhagic Thrombocytopenia in Childhood: A Clinical Study of Twenty-One Cases, J. A. M. A. **98**: 387-393 (Jan. 30) 1932.

In general it may be said that both the white and the differential counts were within normal values, though a polymorphonuclear leukocytosis of over 80 per cent occurred in two instances.

It will be seen that the one constant factor among the initial blood values was the thrombocytopenia. By the very nomenclature of the disease this is, of course, a primary requisite for diagnosis. With a single exception, all platelet determinations recorded in this paper were performed by a small group of permanent members of the hematology department of the hospital. All other platelet counts, including those performed by interns, were discarded as unreliable. We feel, therefore, that our platelet values are as nearly accurate as is possible in a series of this nature. Of the remaining factors included in tables 1 and 2, the same cannot be said. We do feel, however, that the blood count values (red cell, white cell, hemoglobin and differential) as

TABLE 3.—*Results in Cases in Which Operation Was Performed*

Case	Age at Operation	Duration Before Operation	Type	Severity at Operation	Preoperative Transfusions	Postoperative Platelet Rise*	Subsequent Clinical Course	Follow Up	End Result
1	17	53 mos. intermittent	Chronic	Moderate	1	180,000 3d day	Marked improvement 1st 6 mos.; severe recurrence 18th month	18½ mos.	Died 18th month of cerebral hemorrhage
2	47	"All her life" intermittent; 3 mos. continuous	Chronic	Moderate	None	100,000 6th day	Asymptomatic past 10½ years	11 yrs.	Apparently permanently arrested
3	25	"For years" intermittent	Chronic	Mild	None	350,000 30th day	Asymptomatic except for occasional easy bruising and a questionable vaginal hemorrhage	9½ yrs.	Improved; subject to mild recurrences
4	13	10 yrs. intermittent	Chronic	Severe	3	None	Moderately severe purpura for 8½ yrs. following operation; asymptomatic since	9 yrs.	Markedly improved; excellent late result
5	13	8 yrs. intermittent	Chronic	Moderate	None	360,000 9th day	Asymptomatic since operation	7½ yrs.	Apparently permanently arrested
6	11	2 months	Incipient	Moderate	1	500,000 6th day	Asymptomatic except for occasional mild epistaxis	6 yrs.	Markedly improved; excellent result
7	33	10 yrs. intermittent; 3 mos. continuous	Chronic	Severe	3	None	Asymptomatic after 1st 16 mos. except for occasional black and blue spots	3½ yrs.	Markedly improved; excellent result
8	40	5 yrs. intermittent; 6 mos. continuous	Chronic	Moderate	None	89,000 7th day	Asymptomatic except for mild skin purpura on last follow-up visit	3 yrs.	Markedly improved; excellent result
9	15	7 yrs. intermittent; 6 mos. continuous	Chronic	Severe	1	356,000 2d day, 1,025,000 6th day	Asymptomatic since operation	2½ yrs.	Apparently permanently arrested
10	54	5 yrs. intermittent	Chronic	Moderate	1	343,000 4th day 601,000 8th day	Asymptomatic since operation	1 yr.	Apparently permanently arrested

* Figures represent peak of rise occurring prior to discharge.

performed by the intern staff are sufficiently accurate for the purpose of this paper. Some of the figures for bleeding time, clotting time and clot retraction, particularly the first two, are undoubtedly open to question, and it is our opinion that these determinations should be done, whenever possible, by trained technicians. Unfortunately such was not the case in the large majority of instances in our series, and this, we think, may partly explain the appearance in our tables of a clotting time which was unduly prolonged and several bleeding times which closely approach the normal.

Blood groupings were done in thirteen of the twenty-one cases. Of these eight were OI, two were AII, and three were BIII. None were in the ABIV group.

PATHOLOGIC CHANGES

It is generally conceded that the spleens removed in this group of thrombocytopenic purpuras are singularly free from constant pathologic characteristics and, as might have been expected, nothing of unusual interest was brought to light on examination of the ten spleens removed at operation in this series.[20] In only one instance (case 21) was a culture made of the spleen, and in this case a nonhemolytic streptococcus was recovered. Necropsy was not performed on the one patient who died in the operative group. Postmortem examination on the single fatal case in the control group disclosed massive subdural, subarachnoid and cerebellar hemorrhages which were both old and new; extensive extravasations of blood into the majority of the abdominal organs; a bone marrow that appeared normal except for slight hyperplasia; congestion and small areas of hemorrhage in the lymph nodes, and hemorrhage into the splenic follicles with some thickening and hyalinization of the capsule of the spleen.

POSTOPERATIVE COURSE

Of the ten patients who underwent splenectomy in this series, only three had postoperative courses that were entirely uneventful. The complications occurring in the remaining seven cases were as interesting as they were varied. Patient 1 remained in severe shock for the first twenty-four hours after operation but thereafter had a smooth convalescence. Patient 2 did well throughout her postoperative course except for two severe nasal hemorrhages on the sixteenth and twentieth days. Patient 3 developed a bronchitis shortly after operation and on the fifth day had a massive collapse of the left lung, which in turn was followed by a wound disruption (without evisceration) on the ninth day. For the first forty-eight hours after operation, patient 6 was in marked acidosis with acetone breath and acetonuria. Accompanying this he had a pronounced tachycardia. These complications had disappeared by the third day and did not reappear. The postoperative course in case 7 was marked by the development of a brief period of mental aberration and emotional instability. This was thought to be due either to iodoform

20. It is interesting however that, in the operative notes, enlargement of the spleen was reported in all but three cases.

poisoning from the anteoperative packing of the vagina or to cerebral hemorrhage. Shortly after operation, patient 8 developed an unexplained area of skin gangrene in the right lower quadrant. The involved skin subsequently sloughed away and the lesion was pinch grafted. Bacteriologic examination failed to reveal symbiotic or hemolytic organisms. The last patient in the operative group (case 10) developed pneumonia in the left lower lobe on the third day after operation. Resolution was delayed, considerably prolonging her subsequent convalescence.

It will be seen from the foregoing that the series of complications was long and in certain cases rather unusual. Whether or not this was pure coincidence is difficult to say. We do feel, however, that in our small series the postoperative course following splenectomy had more than the number of unexpected and unexplained complications usually seen in a series of equal size in which the operations were of a similar magnitude.

entirely asymptomatic since discharge from the hospital, though in one of the five the platelet level has remained consistently low. The discrepancy between the platelet level and the clinical bleeding illustrated in this last case has been commented on by many observers. In at least four other cases the reverse was true; i. e., mild intermittent purpura was occasionally seen throughout the subsequent follow up despite a normal or even slightly elevated platelet count.

In one case in which the platelets did not respond to operation the patient continued to have moderately severe purpura for eight and a half years and then, following pregnancy, all symptoms ceased, though the platelet count remained low. The one death reported in this series occurred eighteen months after operation from cerebral hemorrhage. It is of interest that in this case splenectomy was followed by a brief rise in the platelets to 180,000 on the third day. Subsequently a fall to below 80,000 ensued, and this figure was never exceeded thereafter. The disease was arrested for

TABLE 4.—*Results in Cases in Which Operation Was Not Performed*

Case	Age on Admission	Duration	Type	Severity	Transfusions	Subsequent Clinical Course	Follow Up	End Result
13	40	3 months	Incipient	Severe	10	Intermittent mild purpura for 11 yrs.	11 yrs. (by letter)	Improved
14	33	6 months	Incipient	Moderate	None	Moderately severe purpura 1st year, thereafter mild	6 yrs.	Improved
15	11	6 months intermittent, 3 weeks continuous	Incipient	Moderate	1	Severe flareup 4th week	26 days	Died of cerebral hemorrhage 26 days after admission
16	19 Outpatient department	6 years intermittent	Chronic	Mild	None	Mild intermittent purpura for 5 years	5 yrs.	Unimproved
17	35	"Since childhood" intermittent, 3 weeks continuous	Chronic	Mild	None	Asymptomatic past 2½ years	4½ yrs.	Spontaneously arrested
18	46	4 days	Incipient	Moderate	7	Asymptomatic past 3 years	3½ yrs.	Spontaneously arrested
19	39	"All her life" intermittent	Chronic	Mild	None	Mild intermittent purpura for 4½ years	4½ yrs.	Unimproved
20	51 Outpatient department	39 years intermittent	Chronic	Moderate	None	Moderately severe intermittent purpura for 2 yrs.	2 yrs.	Unimproved
21	29	1½ years intermittent	Chronic	Moderate	1	Moderately severe intermittent purpura for 2 yrs.	2 yrs.	Unimproved
22	26	5 days	Incipient	Moderate	1	Asymptomatic for past 23 months	2 yrs.	Spontaneously arrested
23	51 Outpatient department	"Since birth" intermittent	Chronic	Mild	None	Intermittent mild purpura for 1 yr.	1 yr.	Unimproved

BLOOD PICTURE FOLLOWING SPLENECTOMY AND SUBSEQUENT CLINICAL COURSE

In all but three of the splenectomized group there was a platelet rise following operation that reached 100,000 or better. Generally speaking the rise was initiated within forty-eight hours of operation and reached its peak within the first ten days. In one instance, however, the rise was delayed and the peak not reached until thirty days subsequent to operation. The height of the rise in all but two cases exceeded 300,000 and in one case reached 1,025,000 six days after operation. In every instance in which a rise took place it was followed by a secondary fall of varying magnitude, and in two of these seven cases the fall carried the platelets below 100,000. There were three cases in the group whose platelets remained at a low level throughout their subsequent follow up, though two of these had a temporary rise following operation. In every instance there was a varying degree of improvement in the clinical symptoms of the disease immediately following splenectomy. In five of the cases all evidence of hemorrhage ceased within seventy-two hours of operation, in at least two it ceased immediately after the procedure. Five cases have been about eight months after operation, but the patient later died in a fulminating recurrence.

It seems appropriate to call attention here to the fact that, following splenectomy, one of our patients gave birth to a child with all the classic signs and symptoms of thrombocytopenic purpura (case 4).

Course in Cases in Which Operation Was Not Performed (subsequent to admission to the hospital or outpatient department).—The first of these cases was admitted to the hospital prior to the era when splenectomy became a generally accepted therapeutic measure in thrombocytopenic purpura. This patient left the hospital with the disease largely arrested, her symptoms having apparently been partially controlled by radium sterilization and ten transfusions (case 13). After discharge she moved to another part of the country but has continued to suffer with the disease, though in mild form. Case 14 yielded sufficiently to eradication of foci of infection in the teeth and x-ray sterilization so that contemplated operation seemed no longer necessary. This patient, however, still has the disease in a mild form. Case 15 was a singularly deceptive one. During the first admission to the hospital the purpura yielded so well to conservative therapy that splenectomy

was not considered necessary. Shortly after leaving the hospital, however, the patient had a fulminating exacerbation of the disease and was readmitted within a week in a moribund condition. She lived for less than one hour after admission, and necropsy revealed that death had been due to cerebral hemorrhage. In case 18 splenectomy was deferred because a leukopenia cast temporary doubt on the diagnosis. After seven transfusions the patient had improved so markedly that splenectomy was felt to be superfluous and within eight

TABLE 5.—*Totals in the Two Groups*

	With Operation	Without Operation	Totals
Completely arrested	4	3	7
Markedly improved	4	0	4
Improved	1	2	3
Unimproved	0	5	5
Died	1	1	2
Totals	10	11	21

months of the onset of the disease a spontaneous arrest occurred which persisted throughout the subsequent follow up. In case 20 splenectomy was obviously the therapy of choice, but the patient repeatedly refused operation and even refused to enter the hospital for observation. The severity of her symptoms since her first visit to the outpatient department has remained essentially unchanged. In case 21 splenectomy was decided on, but the patient changed her mind and refused operation. Throughout her subsequent course no improvement in her condition has been noted.

Two cases, 16 and 23, were ambulatory and have not thus far required hospitalization despite the fact that their mild purpura continues unabated to the best of our knowledge. Of the three remaining cases, all were studied in the hospital at least once and operation was considered but rejected on account of the mildness of the symptomatology. One of the three cases remains unimproved. The other two have become spontaneously arrested. It is of interest that of the entire eleven cases in the group in which operation was not performed the platelet level has returned to a normal figure in only three instances. These three patients are the only ones in the group in which the condition has become spontaneously arrested.

RESULTS

As will be seen from table 5, we have grouped our results for the two series under five headings: arrested, markedly improved, improved, unimproved and died. Under the first category there were four cases in the operative to three in the control group. These cases are apparently definitely arrested. In the "markedly improved" division there are four of the operative to none of the control group. These represent cases which, by reason of an occasional mild symptom or inconsistency in an otherwise perfect follow up, we cannot in conscience include among the definitely arrested. Under the heading of "improved" we have listed one splenectomized and two nonsplenectomized patients. These are individuals who still show persistent evidence of their original disease, but in a milder form. The "unimproved" category needs no explanation. It is significant, however, that there were no cases from the operative group listed under this heading, while the control series was represented by five. One case from each group was fatal. Since the single individual lost in the operative group died eighteen months after operation during an exacerbation of the disease, our operative mortality is zero.

Although we fully realize that in so small a series the validity of statistics is open to question, we have condensed the foregoing observations into the following more readily appreciated figures for purposes of comparison with other series: In the splenectomized group 80 per cent of the cases were vastly improved or arrested, while the same can be said of only 27.2 per cent of the control series. It will be seen further that under improved but by no means arrested we find 10 per cent of the operative and 18.1 per cent of the controls, and that under unimproved or died we find 10 per cent of the splenectomized and 54.5 per cent of the nonsplenectomized. In short, we have found three times as many excellent results among the operative group as among the controls, and five times as many poor results among the controls as among the operative group.

CONCLUSIONS

1. In carefully selected cases of thrombocytopenic purpura, adequately prepared for operation, splenectomy by an experienced surgeon is a highly effective form of therapy, carrying a relatively low operative mortality.

2. The subsequent course of such patients, when compared with their lives previous to operation and with the lives of patients treated by conservative measures, justifies the risks inherent in a major operative procedure.

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THE RÔLE OF CONGESTION (PORTAL HYPERTENSION) IN SO-CALLED BANTI'S SYNDROME

A CLINICAL AND PATHOLOGIC STUDY OF THIRTY-ONE CASES WITH THE LATE RESULTS FOLLOWING SPLENECTOMY

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During the past several years in the Spleen Clinic of the Presbyterian Hospital there have been collected well studied cases of splenomegaly of all types. Many of these were readily classified in one of the several established disease entities. This presentation is an effort to abstract some order out of the large remaining number of cases that had been grouped under the inclusive caption of Banti's disease. As the study developed it became apparent, as it had to many others before us, that we were not dealing with a sequence of clinical and pathologic features as described by Banti. Instead we had an apparently heterogeneous group of cases that presented certain similar characteristics and that shall henceforth be grouped under the name of Banti's syndrome.

As a result of this investigation we shall consider the possibility of a common etiologic factor operating in all these different cases to produce a similar clinical syndrome. The following criteria, as originally laid down by Banti,[1] were drawn on to determine the eligi-

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The clinical and pathologic studies in the two cases of schistosomiasis and the experimental studies referred to in the course of this paper have been carried out at the School of Tropical Medicine under the auspices of Columbia University at San Juan, Puerto Rico. Dr. George Bachman, director, and his staff gave generous assistance in these studies.

1. Banti, Guido: Splenomegalie mit Lebercirrhose, Beitr. z. path. Anat. **24**: 21, 1898; Ueber Morbus Banti, Folia haemat. **10**: 33, 1910.

bility of each particular case for classification within the group. In each individual there was enlargement of the spleen, anemia of varying severity, leukopenia, often intestinal hemorrhages and sometimes ascites. The splenic lesion likewise was consistent with that described by Banti and others and will be discussed more fully in a later section.

This paper will include an outline of the essential features bearing on the diagnosis, on the indications for splenectomy and on the results following operation.

Thirty-one cases comprise the group, and in all splenectomy was performed. These patients all received detailed clinical and hematologic studies before operation and were similarly followed for long periods after operation. The follow up was done at frequent intervals and included the return of the patient for physical examination, complete blood examinations and other studies as indicated.

The thirty-one cases under consideration include all age groups from early childhood to adult life. The division as to sex was even, with sixteen females and fifteen males.

There was no suspicion of a hereditary factor in any of these cases such as one encounters in hemolytic jaundice or Gaucher's disease.

These cases represented a wide ethnologic distribution. We could find no evidence of any racial predisposition. This observation is mentioned only because of the striking racial constancy of some other forms of splenomegaly; namely, erythroblastic anemia and sickle cell anemia.

With the subsequent three exceptions, a careful inquiry into the past health of each of these patients failed to uncover any specific disease entity or other factors that might be the precursor of the splenic lesion. Two patients had the late visceral form of schistosomiasis mansoni with hepatosplenomegaly. In a third patient the following interesting sequence of lesions developed while he was under observation: After a severe abdominal injury a pseudocyst of the pancreas developed. This was operated on. At this time the spleen was normal in size and the blood picture was normal. Two years after this operation and three years after the injury he had a sudden severe hematemesis. On examination he was found to have a large spleen, anemia and leukopenia.

SYMPTOMATOLOGY

Although the disease is usually insidious in its onset, its first warnings may appear with startling suddenness. The most frequent complaint is that of a gradually developing weakness. By far the greatest number of patients in this group, sixteen in fact, declared this to be the initial symptom. Next in frequency and usually most distressing, is the gradual enlargement of the abdomen. Twelve of the group noticed this first. In two of these, distinct mention was made of feeling a lump on the left side of the abdomen. The prominent abdomen in these cases is usually the result of the splenomegaly or ascites or both these factors.

Probably the most alarming sign to the patient, and assuredly the most serious from the point of view of prognosis, is the onset of hematemesis. In eleven instances the individual was unaware of the illness until the sudden appearance of bloody vomitus. Some had only one such experience and others had it on numerous occasions. Hematemesis proved to be the first indication of the disease in six cases, while in five others it appeared later in the course. It is interesting to analyze these cases separately. Hematemesis occurred in four of the cases of the Laënnec type of cirrhosis, in the one case of cavernomatous transformation of the portal vein, in one case of thrombosis of the splenic vein, and in four cases in which no "obstructive mechanism" was demonstrable.

Klemperer,[2] in reviewing the literature on the rare condition of cavernomatous transformation of the portal vein, reported twenty-three cases with nine instances in which hematemesis took place.

It is obvious that portal congestion and the development of esophageal varices do occur in the absence of liver cirrhosis and may be the result of other pathologic conditions.

The longest span over which hematemesis occurred prior to operation in this series was in a case in which it occurred twice in three years. Brahme[3] reported a case of splenic vein thrombosis with repeated hematemeses over a period of forty-five years.

Pain was a fairly frequent complaint and appeared in thirteen, or 42 per cent, of the group. The type, severity and location of the pain are usually dependent on the underlying pathologic lesion. Pain was present at some time in both cases of thrombosis of the splenic vein. This was severe and was located in the epigastrium or left hypochondrium and did not radiate. Besides this intense type of pain, mild epigastric, left upper quadrant and sometimes generalized abdominal pain occurred. The discomfort in some instances was apparently due to the increased weight of the spleen alone. A perisplenitis usually gave sharp pain, aggravated by deep respiration and often with an audible friction rub.

Digestive disturbances were not infrequent. Anorexia and associated weight loss occurred in six instances. Periods of nausea and vomiting were complained of by three patients. Epigastric fulness proved very distressing to three others of the group. Belching, sour eructations or diarrhea were rarely noted.

Epistaxis occurred frequently in five of the cases. There seemed to be no relation between this bleeding tendency and the platelet level. This symptom did not recur following splenectomy except in one of the cases of schistosomiasis, and this patient had only one slight nosebleed following operation. In none of these individuals was there any other hemorrhagic manifestation.

Symptoms referable to the urinary tract were rare. One woman's chief complaint was that of urinary incontinence. She had previously had a perineorrhaphy without relief of this symptom. Following the removal of a very large spleen, this distressing feature was immediately relieved and has remained so. Presumably this was caused by the enlarged spleen pressing on the bladder. It has been something of a surprise to us to find that urinary symptoms are not more frequent.

Cardiac symptoms are seldom seen in the disease. In three cases presenting severe anemia and no apparent heart lesion, dyspnea occurred. Palpitation and precordial distress were present in one case.

We have not been able to correlate symptomatology with the stage of the disease. Patients frequently present themselves with few symptoms and at operation a combination of several advanced lesions is found.

2. Klemperer, Paul: Cavernomatous Transformation of the Portal Vein, Its Relation to Banti's Disease, Arch. Path. **6**: 353 (Sept.) 1928.
3. Brahme, L.: Ein fall von chronischem Portahinderniss, Acta med. Scandinav. **61**: 175, 1924.

LABORATORY EXAMINATION

Most of the routine laboratory procedures were of negative diagnostic value with the exception of the blood count.

The fragility test, bleeding time, clotting time and clot retraction were all within normal limits. Serologic evidence of syphilis was present in only one of the thirty-one cases. Quantitative serum bilirubin determinations showed increased values in only a few cases presenting severe liver damage.

The enumeration of the various cellular elements in the blood was the procedure of greatest diagnostic value. The usual changes included anemia, leukopenia and sometimes thrombocytopenia. The anemia was usually of the secondary, normocytic, hypochromic type. However, in one case of schistosomiasis a macrocytic anemia was present. This has been noted by Wintrobe [4] in other forms of liver cirrhosis, and Rodriguez-Molina [5] has described it in schistosomiasis.

In the absence of complicating hemorrhage we have been unable to correlate, as did Banti, the degree of the anemia with the stage of the disease. A leukopenia was usually the rule except following intestinal hemorrhage, when a transient leukocytosis takes place.

Thrombocytopenia was observed in 40 per cent of the cases and occurred with equal frequency in the presence of Laënnec's cirrhosis, unclassified cirrhosis, schistosomiasis or thrombosis of the splenic vein, or in the group without any demonstrable "obstructive factor." Rosenthal [6] has attempted to subdivide Banti's disease according to the platelet level and speaks of the "thrombocythemic" and "thrombocytopenic" forms.

Following operation, a definite rise took place in the level of the various blood elements. This change in the blood picture will be more fully discussed in a later section.

PATHOLOGY

I shall consider the morbid anatomy of our clinical material under three separate headings: (1) the portal vascular bed, (2) the spleen and (3) the "obstructive factor." I use the term morbid advisedly, as the clinicians comprising our spleen clinic have been as much interested in the local lesion in the living subject as they have been in the examination of fixed tissues later.

1. *The Portal Vascular Bed.*—Any one with experience in splenectomy in this syndrome cannot fail to be impressed by the abnormal conditions as observed during operation. The portal and splenic venous channels usually show moderate to marked dilatation of the various radicles. It is this dilated and often tortuous collection of veins in the splenic pedicle that makes removal of the spleen in these patients such a formidable or often impossible procedure. The rich collateral circulation in the adhesions surrounding the spleen also contributes in no small measure to the hazards of operation. The veins in the splenic pedicle in some of our cases often reached a diameter from two to four times their normal caliber. This local vascular condition was present regardless of the nature of the "obstructive factor" in any particular case. Thus the dilated venous channels were seen in the Laënnec cirrhosis group, were a constant finding in our schistosomiasis cases and were obvious in the patients with splenic vein thrombosis and in the larger group in which the "obstructive factor" could not be demonstrated. The existence of this tense dilated vascular bed in our fifteen cases in which splenomegaly occurred without any obvious obstructive mechanism is an apparent paradox that has greatly interested us. McMichael [7] has intimated that a condition of "portal hypertension" can occur in the absence of such gross and late changes as are found in a hobnail liver. He [8] has demonstrated changes in portal venous pressure in cats following the administration of various drugs. Dr. J. L. Caughey of our medical staff recently has been making some interesting studies on venous pressure in the splenic vein of several types of splenomegaly as seen at the operating table. These results, while still in a very incomplete form, have shown a definite rise in the splenic venous pressure in certain cases of hepatosplenomegaly as contrasted with normal readings in cases of hemolytic jaundice. The observations are suggestive, but much more data will have to be collected before any opinions can be safely expressed. McMichael believes that the thickening of the splenic and portal veins and also the periellipsoidal hemorrhages in the spleen are the anatomic expression of "portal hypertension." I have stressed this section on the portal vascular bed because I believe that most previous studies on Banti's syndrome have singularly neglected this important area. Possibly herein lies a clue to the solution of the cause of this confusing syndrome.

2. *The Spleen.*—The spleen in each of these cases was enlarged. From a study of our material there seemed to be no relationship between the size of the spleen, the duration of the disease or the nature of the "obstructive factor." The largest spleen in our series weighed 3,380 Gm. and was one of the "unclassified cirrhosis" cases. The spleen in the late stage of schistosomiasis is reputedly always very large and in our two cases the specimens weighed 1,220 and 1,330 Gm. respectively. Stiven [9] in a study of bilharziasis in Egypt recorded one case in which the spleen weighed 7 Kg.

The gross appearance of the spleen is decidedly different from the small soft organs found in purpura haemorrhagica or hemolytic jaundice. The capsule is thickened and is usually covered with numerous vascular fibrous tabs at the site of adhesions. Hyaline plaques are seen occasionally and infarcts rarely. When the organ is cut a sensation of increased resistance is felt. The pulp is grayish red and neither bulges above nor sinks below the severed capsule. Malpighian bodies are seen with difficulty and seem to be diminished in number. Grayish opaque, thickened trabeculae ramify outward from the hilus. The veins in these trabeculae are usually dilated as one would expect after seeing the hilus vessels.

Our histologic studies, like our gross examinations, again impressed us with the similarity of the changes in the spleen in the various cases. The characteristic features were scarring and the obliteration of the usual architecture. The cellular elements of both red and white pulp were decreased. The fibrosis included capsular and trabecular thickening, together with interstitial fibrosis and so-called fibroadenie of Banti. There was a diminution of the number and size of the mal-

4. Wintrobe, M. M., and Shumacker, H. S., Jr.: The Occurrence of Macrocytic Anemia in Association with Disorder of the Liver, Bull. Johns Hopkins Hosp. **52**: 387 (June) 1933.

5. Rodriguez-Molina, R.: Anemia in Schistosomiasis Mansoni and Its Treatment in Puerto Rico, Am. J. Trop. Med., to be published; read before the American Society of Tropical Medicine, Nov. 20, 1935.

6. Rosenthal, Nathan: Clinical and Hematological Studies on Banti's Disease: The Blood Platelet Factor with Reference to Splenectomy, J. A. M. A. **84**: 1887 (June 20) 1925.

7. McMichael, J.: Local Vascular Changes in Splenic Anemia, Edinburgh M. J. **38**: 1 (Jan.) 1931. The Pathology of Hepatolienal Fibrosis, J. Path. & Bact. **39**: 481 (Sept.) 1934.

8. McMichael, J.: The Portal Circulation, J. Physiol. **75**: 241 (June) 1932.

9. Stiven, H. E. S.: Splenectomy for Egyptian Splenomegaly, Brit. J. Surg. **17**: 230 (Oct.) 1929.

pighian corpuscles. We believe that in general the cellular elements diminish as the disease progresses and that in younger individuals the lymphocytes are proportionately more numerous, as they are in the other lymphoid depots. We believe that the physiologic and pathologic studies of McMichael offer a sound and plausible explanation of the development of the splenic lesion in Banti's syndrome. This author's observations were limited to cases of so-called hepatolienal fibrosis, which type of course forms only a portion of our more inclusive grouping.

Tait and Cashin [10] believe that normally the ellipsoid acts as a capillary regulator protecting the pulp from sudden overflooding and, conversely, preventing reflux of blood back into the arteries. McMichael evaluated the changes in the spleen in hepatolienal fibrosis on the basis of local vascular disturbances. In his original paper and in later publications [7] he postulates that the siderotic nodule, the periarterial fibrosis, and the "fibroadenie" of Banti are all one and the same thing. These three terms are synonymous for a lesion that is the end result of hemorrhages around the ellipsoidal capillaries, and not, as Banti believed, inflammatory in origin. The only cases in our series showing this supposedly early lesion were the two cases of splenic vein thrombosis. Each of these spleens in addition to the usual fibrotic picture showed evidence of old and recent hemorrhages usually at the periphery of the malpighian body. McMichael believed that in addition to venous congestion one other factor was necessary to produce splenomegaly in hepatolienal fibrosis. This hypothesis will be more fully considered in the next section.

3. *The "Obstructive Factor" and Its Relation to Portal Congestion.*—While discussing the factors in our cases which we consider significant in the development of Banti's syndrome, we shall present the negative as well as the positive evidence at our command and review some of the varying opinions that have been expressed from time to time.

Banti believed that the disease originated primarily in the spleen, with toxins acting directly on this organ. As a result, a splenomegaly developed. Following this, the disease passed through a transitional stage and ended with cirrhosis of the liver. This opinion has been perpetuated in this country in such standard textbooks as those of Osler [11] and Cecil.[12]

Eppinger [13] in his classic treatise on hepatolienal diseases recognized the influence of venous stasis in the production of what the German school has called "stauungsmilz." He cites the earlier writings of Cauchois, enumerating an almost endless list of lesions that might conceivably produce obstruction of the portal bed and secondary splenomegaly.

Warthin [14] and again Eppinger [13] emphasized the striking clinical similarity between Banti's disease and the splenomegaly that develops secondary to chronic splenic vein thrombosis. Similar observations with case reports have been recorded by Brahme,[3] Wallgren [15] and Göttche.[16]

McNee [17] believed that portal stasis may play a part in Banti's disease but that there is little or no clinical or experimental evidence to support this view. Both McNee and McMichael have consistently maintained that the factors of increased portal pressure and the entry of toxic substances in the portal circulation are the best possible explanations.

Larrabee [18] in a recent paper has expressed the view that Banti's syndrome is the result of various intra-abdominal lesions obstructing the venous outflow of the spleen.

Messimy [19] has attempted to differentiate the splenic picture in Banti's disease from that in the usual Laënnec cirrhosis. He considers the essential lesion in the spleen in the cirrhosis cases to be the result of portal stasis

Chart 1.—Follow-up results of splenectomy in Banti's syndrome.

with back pressure in the splenic veins. In Banti's disease the process is periarterial in the spleen and is inflammatory in nature.

In our series we have fifteen cases in which either at the time of operation or subsequently no obstructive mechanism could be demonstrated. These fifteen cases showed no evidence of cirrhosis and because of the limited exposure at operation a detailed examination of the portal bed was obviously impossible. This group of cases presents the widest gap in our evidence to support the theory of venous obstruction as the causative agent.

The remaining sixteen cases included nine cases of Laënnec cirrhosis, two cases of unclassified cirrhosis, two cases of schistosomiasis, two cases of thrombosis

10. Tait, J., and Cashin, H.: Some Points Concerning the Structure of the Spleen, Quart. J. Exper. Physiol. **15**: 421, 1925.
11. Osler, William: Principles and Practice of Medicine, ed. 12, New York, D. Appleton-Century Company, 1935.
12. Cecil, R. L.: Textbook of Medicine, Philadelphia, W. B. Saunders Company, 1928.
13. Eppinger, H.: Die Stauungsmilz beim Menschen: Die Hepatolienalen Erkrankungen, Berlin, Julius Springer, 1920, pp. 384-493.
14. Warthin, A. S.: The Relation of Thrombophlebitis of the Portal and Splenic Veins to Splenic Anemia and Banti's Disease, Internat. Clin. **4**: 189, 1910.
15. Wallgren, A.: Contribution à l'étude des splénomégalies de l'enfance, Acta Paediat. (supp.) **6**: 1-122, 1927.
16. Göttche, O., and Vertán, E.: Ein fall von Milzvenenstenose, Jahrb. f. Kinderh. **12**: 221 (April) 1930.
17. McNee, J. W.: Lettsomian Lectures, Lancet **1**: 951 (May 2), 1009 (May 9), 1063 (May 16) 1931.
18. Larrabee, R. C.: Congestive Splenomegaly and Its Relation to Banti's Disease, Am. J. M. Sc. **188**: 745 (Dec.) 1934.
19. Messimy, R.: Contribution à l'étude des réticulo-fibroses de la rate, Ann. d'anat. path. **12**: 85 (Jan.) 1935.

of the splenic vein, and one case of cavernomatous transformation of the portal vein.

In seven of the nine cases of Laënnec cirrhosis and the two unclassified cirrhoses the diagnosis was confirmed by liver biopsy.

In our two cases of splenic vein thrombosis, one was post-traumatic and the other was without known cause. In both of these, venous dilatation occurred proximal to the occluded vessels.

One of our youngest patients had a most unusual lesion. At necropsy within two days following splenectomy a cavernomatous transformation of the portal vein was found. Marked dilatation of the splenic and gastric veins was observed and death was due to the rupture of esophageal varices.

Klemperer [2] reported a case of this rare condition and collected twenty-two additional examples. Of these twenty-three cases, twenty-two presented splenomegaly and all showed varying degrees of occlusion of the portal or splenic veins. Klemperer's patient had had a splenectomy for supposed Banti's disease several years prior to death.

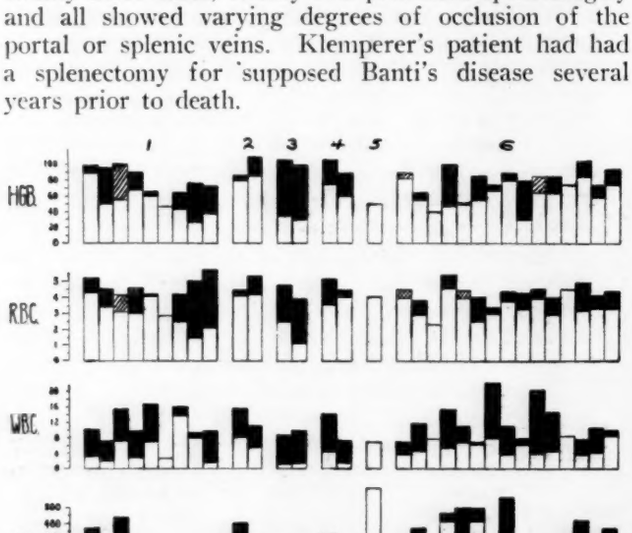

Chart 2.—Preoperative blood counts are represented by unshaded blocks. The postoperative blood values (increment or decrement) at the time of the last follow-up visit are represented as shaded or cross-hatched blocks.

The two cases of schistosomiasis mansoni in our group represent the first two of a larger series to be reported by Dr. Whipple in a subsequent paper. The mode of infection and the pathology of bilharziasis are now well known. Faust, Jones and Hoffman [20] have shown that the maturing phase of the parasite in the human host takes place in the hepatic, portal and mesenteric veins. Following deposition of eggs in the liver, a pseudotubercle or fibrous nodule is formed. If the infestation is sufficiently heavy, a severe form of cirrhosis results. Coupled with this cirrhosis is a splenomegaly, and with the hepatosplenomegaly there is often a blood picture similar to that in Banti's syndrome. Oddly enough, this striking similarity of Banti's disease to the late visceral stage of schistosomiasis mansoni is one that has received scant mention. Bonelli [21] drew the clinical comparison but concluded that the Banti-like picture in late schistosomiasis was on the basis of a toxin of intestinal origin. Girges [22] with his extensive experience in Egyptian splenomegaly includes Banti's disease as a differential diagnosis of the late stage of the disease.

During the past several years, those working in the Spleen Clinic have been conducting clinical and experimental studies in Puerto Rico, where schistosomiasis is endemic. We have been interested in studying the development of the hepatosplenomegaly under conditions in which a known parasite is the inciting cause of the liver cirrhosis. At operation in the two cases reported herein, a severe grade of liver cirrhosis was apparent and was proved by biopsy.

In summary, therefore, in our thirty-one cases there were fifteen in which no "obstructive factor" could be demonstrated at operation. Thirteen cases presented some form of liver cirrhosis. Two cases presented thrombosis of the splenic vein, and one a cavernomatous transformation of the portal vein.

THE RESPONSE TO SPLENECTOMY

All the cases recorded in the foregoing sections have been followed carefully and the response to splenectomy will be considered according to groups and in each instance the hematologic observations will be reviewed, the preoperative being compared with the postoperative level.

The follow-up results in the various groups can be traced in chart 1. The cases are retained in the groupings as previously described: (1) Laënnec cirrhosis, (2) unclassified cirrhosis, (3) schistosomiasis mansoni, (4) thrombosis of the splenic vein, (5) cavernomatous transformation of the portal vein, (6) obstructive factor not demonstrated.

It is immediately apparent that the poorest results appear in the group having Laënnec cirrhosis. There were nine cases presenting the combination of this type of cirrhosis and Banti's syndrome. The immediate hospital mortality included two cases, or 22 per cent. One of these patients died of hematemesis and one of surgical shock. The remaining five fatalities occurred in periods varying from three months to thirteen years. Four patients succumbed to severe hematemeses and the fifth had recurring ascites and died of hepatic insufficiency. In spite of the poor late results, 66 per cent of the group were well from periods varying from two to thirteen years following operation.

The outcome of the succeeding groups was obviously much more encouraging. The patients having the unclassified type of cirrhosis, schistosomiasis mansoni or thrombosis of the splenic vein have all done exceedingly well. As is seen in chart 1, these individuals have been entirely symptom free and have remained well for long periods.

The one patient with cavernomatous transformation of the portal vein had had repeated hematemeses for two years prior to operation and promptly succumbed to a similar massive hemorrhage forty-eight hours after operation.

Our last series of fifteen cases in which the "obstructive factor" could not be demonstrated gave a hospital mortality of two cases, or 13 per cent, and a late mortality of three cases, or 20 per cent. The remaining ten patients (66⅔ per cent) have with one exception continued in excellent health for periods up to ten

20. Faust, E. C.; Jones, C. A., and Hoffman, W. A.: Studies on Schistosomiasis Mansoni in Puerto Rico: III. The Mammalian Phase of the Life Cycle, Puerto Rico. J. Pub. Health & Trop. Med. **10**: 133 (Dec.) 1934.

21. Bonelli, P.: Analogia entre la schistosomiasis mansoni y la enfermedad de Banti o anemia esplénica, Bol. Asoc. méd. de Puerto Rico **23**: 251 (July) 1931.

22. Girges, Rameses: Schistosomiasis, London, John Bale, Sons and Danielsson, Ltd., 1934.

years.[23] The single exception has had a miserable clinical course punctuated by repeated hematemeses over a span of ten years and is still alive. The cause of death in the last series included one case each of hematemesis, hepatic insufficiency, brain cyst, cerebral thrombosis and surgical shock.

From the foregoing experience one is immediately impressed with the gravity of hematemesis as a prognostic sign. Of the eleven patients who had evidence of esophageal hemorrhage prior to operation, seven died of the same complication. We have accordingly accepted hematemesis as an ominous symptom and feel that in this type of case operation should be avoided.

Although thrombotic phenomena are reported as being frequent sequelae of splenectomy in Banti's syndrome, only one patient in this study had this complication. Rosenthal [6] has emphasized the danger of thromboses after splenectomy in the "thrombocythemic" form of Banti's disease. Our experience does not confirm this observation. Graham Bryce [24] has shown that an apparently unsuitable case with a normal platelet count can be safely steered through the danger of splenectomy and, conversely, a low platelet count prior to operation does not necessarily protect the patient from fatal thrombosis.

As a parallel to the clinical improvement in our cases there has also been a favorable response in the blood picture. From chart 2 it is seen that, following splenectomy, there is usually a rise of the erythrocyte count, the hemoglobin content and the leukocyte and platelet levels. The groups as listed 1, 2, 3 and so on correspond directly to the same numbered groupings in chart 1. It is of interest to note that the total leukocyte count usually remains at a fairly high level throughout life, averaging 12,000 per cubic millimeter.

COMMENT

Reviewing the previous data, we wish to stress the clinical sequence of events of three cases in which there is adequate knowledge of the etiology and progress of the disease.

The two cases of schistosomiasis presented the classic features of the visceral stage of the disease. The pathogenesis and pathology of this disease are now well known. In such cases as we have described, there is a cirrhosis of the liver and splenomegaly. The cirrhosis follows pseudotubercle formation around ova deposited in the liver. The parasite rarely reaches the spleen except in overwhelming infestations. In spite of the absence of ova in the spleen, a scarring of this organ occurs. Although the splenic picture has been explained on the basis of toxins liberated by the parasites as they inhabit the portal and mesenteric veins, we believe that the splenomegaly can be secondary to the liver cirrhosis and the resultant portal venous congestion. It is certainly noteworthy that this tropical disease can in its late stages so well mimic Banti's disease.

The third case of interest to us is one in which we had the good fortune to have the clinical picture develop under our own observation. The history of this individual included a severe abdominal injury, followed by the development of a traumatic pseudocyst of the pancreas. This was operated on two years after the injury. At this time the spleen was not enlarged and the blood picture was normal. One year later (three years after the injury) the patient began to have severe pain in the left upper quadrant, weakness and then suddenly a hematemesis. At this time it was found that the spleen was markedly enlarged and that the blood changes were consistent with a diagnosis of Banti's syndrome. At operation, occluded splenic veins were palpable.

These three cases have been separately emphasized, as they seem to be supporting links in our chain of evidence to show that at least in some cases of Banti's syndrome a primary obstructive factor exists.

SUMMARY

In a group of thirty-one cases, similar characteristics were apparent. In all, a state of venous congestion existed, as was evidenced by the dilated, tense venous channels in the portal or splenic bed.

There were sixteen instances in which a specific "obstructive factor" could be demonstrated as the possible agent producing venous stasis. However, in fifteen cases no evidence of an obstructive mechanism could be found.

A state of "portal hypertension" probably is present in all cases of Banti's syndrome. Splenic venous pressure determinations have been done in a few selected cases. These have been consistently higher than the peripheral venous pressure.

Our clinical and pathologic studies have led us to believe that in some cases this "portal hypertension" is secondary to the various obstructive lesions as described, whereas in other cases this may occur, as intimated by McMichael, as a primary disturbance of the portal system without a visible obstructive factor.

We believe that the mechanical interference with the splenic circulation may result in so-called congestive splenomegaly. This in turn may affect the activity of blood formation with depression of the cellular elements in the blood.

Following splenectomy in any of the groups previously discussed, this inhibitory effect is apparently removed, permitting a gradual return of the blood values to normal.

The indications for splenectomy and the long term prognosis are dependent on the nature and severity of the "obstructive factor." Obviously splenectomy is contraindicated in the presence of severe liver damage. The late results of splenectomy in our cases with Laënnec cirrhosis have been poor. The results in the remaining groups of cases have been most encouraging.

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23. Since the completion of this paper we have again seen patient 9 in group 6. It has now been sixteen years since the splenectomy. The patient is in excellent health; physical examination is negative and all blood values including the platelet count are normal.

24. Graham Bryce, A.: Splenectomy and Thrombosis, Lancet **2**: 1423 (Dec. 31) 1932.

Expert Witness.—By the middle of the seventeenth century (in England) . . . the expert, possessed of a certain skill and knowledge, ceased to be an adviser to the court and was presented by one side or the other as a witness to the jury. Thus, although the value of his knowledge was still recognized, he had now become a partisan, at least in the eyes of the jury. In view of the contentious nature of legal proceedings, it was to be expected that counsel would present only experts favoring their particular thesis. Quite aside from honest differences of opinion, the possibility of bias must be recognized, and the unfortunate though rarer incidence of venality must be admitted. On the whole, it is not strange that the method of partisan introduction of expert evidence has brought suspicion on experts in general, and that as long ago as 1843 we find an English court saying "Hardly any weight is to given to the evidence of what are called scientific witnesses; they come with a bias in their minds to support the cause in which they are embarked." (Tracy Peerage Case, 10 Cl. & F., 154.)—Overholser, Winfred: The Place of Psychiatry in the Criminal Law, *Psychiatric Quarterly* **10**:197 (April) 1936.

RATE OF EXCRETION AND BACTERICIDAL POWER OF MANDELIC ACID IN THE URINE

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Last year we[1] presented data to show the minimal concentration of oxybutyric acid in urine and the optimal p_H of urine that were necessary to cause sterilization of urine that had been inoculated with various strains of organisms isolated from urine. This acid results from the incomplete combustion of fats when only extremely small amounts of carbohydrate are given. The so-called ketogenic diet is difficult for many people to take. Recent work originating in England and pioneered by Rosenheim[2] has resulted in the knowledge that mandelic acid, when administered orally, escapes metabolism or conjugation in the animal organism and is excreted in the urine by the kidney in a concentration sufficient for bactericidal action, provided the p_H of the urine is lowered simultaneously. This acid was chosen as a result of experiments with many organic acids.

TABLE 1.—*Rate of Excretion of Mandelic Acid and the p_H of the Urine of a Dog Receiving a Continuous Intravenous Injection During Seven Hours of 700 Cc. of 1 per Cent Solution of Sodium Mandelate*

	Urine		
Hours After Beginning Injection	Volume of, Cc.	Concentration of Mandelic Acid in, per Cent	p_H of
2	22	1.5	8.18
4	112	0.98	7.15
6	245	0.50	6.49
7	161	0.50	5.83
Urea clearance after injection: 27.1 cc. per minute		Blood urea after injection: 44 mg. per 100 cc.	
Urea clearance three days later: 57.1 cc. per minute		Blood urea three days later: 30 mg. per 100 cc.	

N. B.: Same as table 1 in Proc. Staff Meet., Mayo Clin. **11**: 374 (June 10) 1936.

Methods for sterilization of urine in cases of infection of the urinary tract are undergoing change and there is a general trend toward establishment of a more simple type of therapy. As yet, the simplest type of therapy has not been found.

In this paper we present data descriptive of our experimentation on animals and of our clinical experience, demonstrating the rate of excretion of mandelic acid following oral ingestion by man and following intravenous injection into dogs of its sodium salt. We also present the result of observations establishing the concentration of acid and the p_H necessary for the urine to possess bactericidal activity against numerous strains of organisms isolated from the urine of individuals having infections of the urinary tract.

Mandelic acid was determined as recommended by Rosenheim. This technic yields slightly high results owing perhaps to extraction of small amounts of other organic acids. However, for the purposes at hand the method is sufficiently accurate. Values for the p_H of the urine were determined by the quinhydrone-electrode technic.

In table 1 are given the rate of excretion of mandelic acid and the p_H of the urine of a dog that had received a continuous injection, during seven hours, of 700 cc. of a 1 per cent solution of sodium mandelate. It is evident that the concentration of mandelic acid reaches a value sufficient for bactericidal activity, provided the p_H of the urine is lowered to a value shown later to be the optimal one for bactericidal activity. The decrease of concentration over a period of seven hours from 1.5 per cent to 0.5 per cent is caused by the diuresis produced by the injection of 700 cc. of fluid. The kidneys of this animal received a temporary insult, as is evidenced by the fact that the urea clearance after injection was lowered to 27.1 cc., with a value for blood urea of 44 mg. per hundred cubic centimeters. This urea clearance increased during the next three days to 57.1 cc., and the concentration of blood urea became 30 mg. in each hundred cubic centimeters. This is evidence of the fact that any injury that may be produced in the kidney is only temporary.

TABLE 2.—*Excretion of Mandelic Acid in the Urine of a Patient Following Oral Ingestion of 5 Gm. of Mandelic Acid*

	Urine	
Hours After First Dose	Volume of, Cc.	Concentration of Mandelic Acid in, per Cent
2	240	0.38
6	240	0.60
10	155	0.61
24	500	0.21

Table 2 demonstrates the excretion of mandelic acid in the urine of a man, following oral ingestion of 5 Gm. of sodium mandelate in one dose. Eighty per cent of the ingested mandelic acid appears in the urine within twenty-four hours and the maximal excretion occurs approximately two hours following oral ingestion of the acid.

Table 3 shows the rate of excretion of mandelic acid and the p_H of the urine of a patient who had ingested 3 Gm. of mandelic acid in the form of a 10 per cent solution of the sodium salt four times during the day, and who also had ingested ammonium choride as an acidifying drug to lower the p_H of the urine. This table illustrates the cumulative excretion of mandelic acid as various quantities are ingested and shows also that, although diuresis may be produced, the concentration of mandelic acid reaches a value in excess of 1 per cent.

TABLE 3.—*Rate of Excretion of Mandelic Acid and the p_H of the Urine of a Patient Ingesting 3 Gm. of Mandelic Acid at Four Different Intervals; Ammonium Chloride Also Was Taken*

	Urine		
Hours After First Dose	Volume of, Cc.	Concentration of Mandelic Acid in, per Cent	p_H of
2	37	0.32	5.0
6	138	0.96	5.0
10	194	0.83	5.0
12	435	1.14	5.0

N. B: Same as table 2 in Proc. Staff Meet., Mayo Clin. **11**: 374 (June 10) 1936.

Table 4 illustrates the concentration of mandelic acid and the p_H of the urine of a patient under prescribed treatment with ammonium chloride and mandelic acid

From the Section on Pediatrics (Dr. Helmholz) and the Section on Clinical Biochemistry (Dr. Osterberg), the Mayo Clinic.

1. Helmholz, H. F., and Osterberg, A. E.: The Bactericidal Effect in Urine of Levorotatory and Racemic Beta-Oxybutyric Acid, Proc. Staff Meet., Mayo Clin. **10**: 620-622 (Sept. 25) 1935; The Bactericidal Effect of Levorotatory and Racemic Beta-Oxybutyric Acid in Urine, J. Urol. **35**: 86-92 (Jan.) 1936.

2. Rosenheim, M. L.: Mandelic Acid in the Treatment of Urinary Infections, Lancet **1**: 1032-1037 (May 4) 1935.

in the form of the sodium salt. This table shows that the p_H of the urine can be lowered to a value of approximately 5.0 over a period of many days while a concentration of mandelic acid in the neighborhood of

TABLE 4.—*Concentration of Mandelic Acid in the Urine and the p_H of the Urine of a Patient Under Treatment with Mandelic Acid and Ammonium Chloride*

	Urine	
Day of Experiment	Concentration of Mandelic Acid in, per Cent	p_H of
1	0.63	
2	1.1	
3	0.91	
4	0.75	5.2
5	0.45	5.0
6	0.90	5.0
7	0.16	5.0
8	0.27	5.1

1 per cent is maintained. These values have been shown to be most conducive to bactericidal activity. On the seventh day of treatment the ingestion of mandelic acid was stopped and the concentration in the urine was accordingly lowered considerably.

The bactericidal power of the urine was determined by the same methods that were employed in our earlier study[1] on beta-oxybutyric acid. Again we want to emphasize that control experiments show that, with the exception of Proteus ammoniae, we have not found gram-negative organisms isolated from urine of patients having urinary infections which were killed by a p_H of 5.0 in the absence of an organic acid (table 5).

The first series of experiments was done with urine from patients who received sodium mandelate, and the concentration of mandelic acid in the urine varied from 0.25 to 1.1 per cent. At a p_H of 5.0, mandelic acid 0.25 per cent is bactericidal for most organisms; at a p_H of 5.3, a concentration of 0.5 per cent is bactericidal, and at a p_H of 5.7 a concentration of 1.0 per cent is bactericidal (table 5). Just as is true of the bactericidal action of beta-oxybutyric acid, the lower the p_H the lower the concentration of acid necessary for bactericidal action. In a series of experiments in which a 1.0 per cent concentration of this acid was added to normal urine and in a series in which the acid was excreted in the urine in a concentration of 1.0 per cent after it had been administered by mouth, the bactericidal action corresponded very closely.

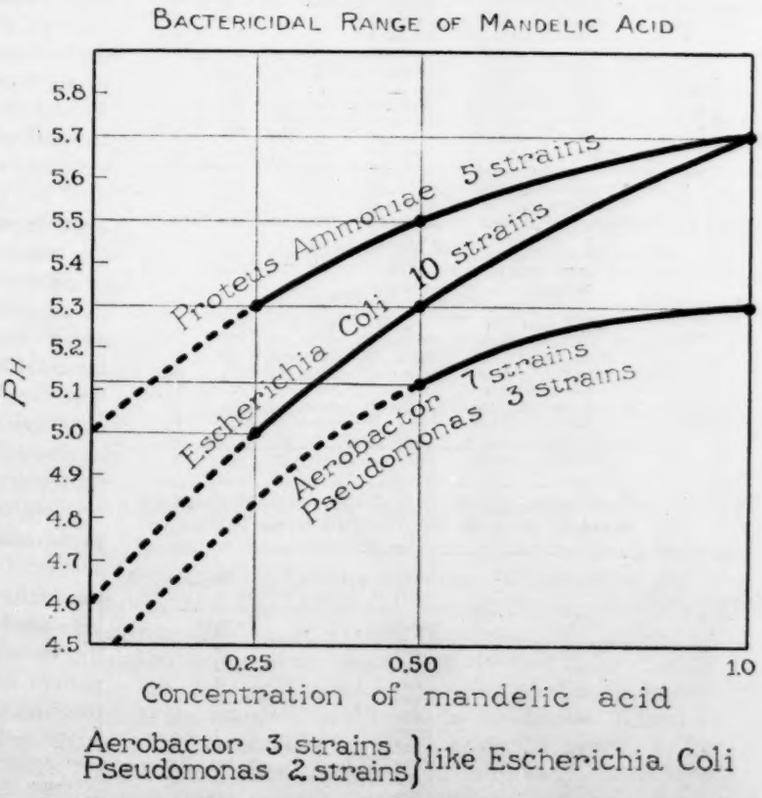
In the great majority of urinary infections the organisms are bacillary in type and in large measure are Escherichia coli, Aerobacter, Proteus and Pseudomonas. It was this group which was studied intensively. Ten strains of Escherichia coli, ten strains of Aerobacter, five strains of Proteus ammoniae and five strains of Pseudomonas were tested with concentrations of 0.25, 0.5 and 1.0 per cent mandelic acid at a p_H varying from 5.0 to 5.7. The strains of Escherichia coli and of Proteus ran true to form, as all the strains were killed at the same concentrations of acid and at the same p_H (tables 6 and 7). The ten strains of Aerobacter could be separated definitely into a group of three strains that were killed under the same conditions of concentration of acid and of p_H as the Escherichia coli and into a group of seven strains that were killed only when the p_H of the urine was the same as that necessary to kill Escherichia coli but the concentrations of acid were higher, or when the p_H of the urine was lower and the concentration of mandelic acid remained the same (table 8). There was one strain that was killed only at a p_H of 5.3 and a concentration of 1.0 per cent mandelic acid. Of the ten organisms, four were motile and six were nonmotile. Of the strains of Pseudomonas, two corresponded to Escherichia coli and three to Aerobacter (table 9).

It is thus evident that Escherichia coli is uniformly killed at a certain p_H and concentration of acid and that

TABLE 5.—*Bactericidal Effect of Urine Excreted by Patients Receiving Sodium Mandelate*

Concentration of Acid in Urine	p_H of Urine	Escherichia Coli	Aerobacter	Proteus	Pseudomonas
0	4.8	—	—	+	+
0	5.0	—	—	+	—
0.25	5.3	—	—	+	—
0.33	5.3	—	—	+	—
0.41	5.42	—	—	+	—
0.60	5.3	+	+	+	+
0.82	5.52	+	+	+	+
1.1	5.37	+	+	+	+

certain strains of Aerobacter and of Pseudomonas are killed at the same concentrations of acid and p_H but that to kill the greater number of strains a higher concentration of acid or a lower p_H is required, or both are required. This no doubt accounts for the conflicting results that various observers have obtained in treating infections with Aerobacter and with Pseudomonas by means of the ketogenic diet. Apparently the organism most easily killed is Proteus ammoniae, as is seen in all the experiments. The acidity of 4.8 alone in some



Relation of concentration of mandelic acid to p_H of urine in the production of bactericidal action. Same as chart in Proc. Staff Meet., Mayo Clin. **11**: 376 (June 10) 1936.

instances completely sterilizes a heavily inoculated urine. The difficulty in the treatment of infections with Proteus is the inability to acidify the urine because of the tendency of Proteus to produce a strongly alkaline reaction in the urine. The accompanying chart shows in a graphic way the relationship of concentration of the mandelic acid and the p_H of the urine in its bactericidal effect for various bacilli.

The bactericidal effect of mandelic acid on a large series of coccus organisms has not been studied but several strains of staphylococci have been tested out in individual experiments and in a general way have been found to correspond, in respect of their vulnerability, to the bacillary group (table 10). Clinically also two patients have been freed from infection with Streptococcus faecalis by treatment with mandelic acid. It will be necessary, however, to make further determinations with a larger series of organisms to see whether they all fall within the same general range.

In conclusion, two facts can be stated: 1. By oral administration of sodium mandelate, concentrations of the acid varying from 0.25 to 1 per cent can be obtained readily in the urine. In this range of concentration the acid will act bactericidally on most organisms at a p_H ranging from 5.0 to 5.7. 2. Certain strains of Aerobacter and Pseudomonas are far more difficult to kill than is Escherichia coli.

TABLE 6.—*Bactericidal Effect of Mandelic Acid on Ten Strains of Escherichia Coli*

Concentration of Acid in Urine	p_H of Urine	Strains									
		1	2	3	4	5	6	7	8	9	10
0.25	5.0	+	+	+	+	+	+	+	+	+	+
0.25	5.3	—*	—	—							
0.5	5.3	+	+	+	+	+	+	+	+	+	+
0.5	5.5	—*	—	—							
1.0	5.5	+	+	+	+	+	+	+	+	+	+
1.0	5.7	+	+	+	+	+	+	+	+	+	+
1.0	6.0	—*	—	—							

* Only three strains.

TABLE 7.—*Bactericidal Effect of Mandelic Acid on Five Strains of Proteus Ammoniae*

Concentration of Acid in Urine	p_H of Urine	Strains				
		1	2	3	4	5
0.25	5.0	+	+	+	+	+
0.5	5.3	+	+	+	+	+
1.0	5.5	+	+	+	+	+
1.0	5.7	+	+	+	+	+

TABLE 8.—*Bactericidal Effect of Mandelic Acid on Ten Strains of Aerobacter*

Concentration of Acid in Urine	p_H of Urine	Strains									
		1	2	3	4	5	6	7	8	9	10
0.25	5.0	+	+	—	—	—	—	—	+	+	—
0.50	5.12	+	+	+	—	+	+	+	+	+	+
0.50	5.3	+	—	—	—	—	—	—	+	+	—
1.0	5.3	+	+	+	+	+	+	+	+	+	+
1.0	5.5	+	+	—	—	+	+	—	+	+	—
Motility		—	—	+	—	—	+	+	—	+	—

TABLE 9.—*Bactericidal Effect of Mandelic Acid on Five Strains of Pseudomonas Aeruginosa*

Concentration of Acid in Urine	p_H of Urine	Strains				
		1	2	3	4	5
0.25	5.0	—	+	+	+	+
0.5	5.12	+	+	+	+	+
0.5	5.3	—	+	—	—	+
1.0	5.3	+	+	+	+	+
1.0	5.5	—	+	—	+	+

TABLE 10.—*Bactericidal Effect of Various Concentrations of Mandelic Acid on the Staphylococcus*

Concentration of Acid in Urine	p_H of Urine	Colonies in 0.5 Cc. Before and After 24 Hours' Incubation	
		Before	After
0.25	5.0	1,280	0
0.25	5.3	1,210	74
0.33	5.13	1,340	3
0.33	5.55	2,400	Innumerable
0.41	5.42	1,420	530
0.43	5.12	2,240	1
0.63	5.65	1,350	2,400
0.67	5.52	2,220	900
0.80	5.52	1,420	340
0.82	5.44	1,980	140
1.1	5.37	1,070	17

MANDELIC ACID AS A URINARY ANTISEPTIC

A CLINICAL STUDY

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It was shown as early as 1917 by Shohl and Janney [1] that the hydrogen ion concentration of urine affected the growth of bacteria, and they demonstrated that colon bacilli were retarded in growth in a urine of p_H 5 or less and on the alkaline side of 9.2 or more. This fact has been utilized in the administration of ammonium chloride followed by methenamine intravenously or orally. The introduction of the ketogenic diet by Clark [2] and by Helmholz [3] in 1931 marked another step in the therapeutics of bacteriuria. Although the patient on a ketogenic diet developed a highly acid urine, it was soon found that the acidity of the urine, though helpful, was not the only factor in bringing about the growth-inhibiting effect but that some bactericidal substance was excreted (Clark, Dick, Helmholz [4]). A. T. Fuller [5] of the Barnhard Baron Memorial Research Laboratories of London started investigation to discover this effective agent. A chemical fractionation was carried out of a mixture of urines that were actively bacteriostatic. The removal of the urea, inorganic salts, phosphatides, proteoses, bases and amino acids did not reduce the bacteriostatic properties. After the lactic acid was removed, the levorotatory form of beta-oxybutyric acid was left, which was found to be the bacteriostatic property in the urine excreted by the patient on the ketogenic diet. Finding the amount of this substance to be small in the ketogenic urine, Fuller suggested giving it by mouth. Investigations carried

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The authors were assisted by Dr. Hollis N. Allen and Dr. S. H. Gray, who performed the bacteriologic work, and Drs. Thomas Saam and James B. Harris, resident urologists, City Hospitals, who managed some of the cases submitted in this clinical study.

1. Shohl, A. T., and Janney, J. H.: The Growth of Bacillus Coli in Urine at Varying Hydrogen Ion Concentration, J. Urol. **1**: 211-229 (April) 1917.
2. Clark, A. L.: Escherichia Coli Bacilluria Under Ketogenic Treatment, Proc. Staff Meet., Mayo Clin. **6**: 605 (Oct. 14) 1931.
3. Helmholz, H. F.: The Ketogenic Diet in the Treatment of Pyuria of Children with Anomalies of the Urinary Tract, Proc. Staff Meet., Mayo Clin. **6**: 609 (Oct. 14) 1931.
4. Helmholz, H. F.: The Ketogenic Diet in the Treatment of Urinary Infections of Childhood, J. A. M. A. **99**: 1305 (Oct. 15) 1932.
5. Fuller, A. T.: Lancet **1**: 855 (April 22) 1933.

out by a number of clinicians demonstrated it to be ineffective, however. As Cook and Braasch[6] commented, "Theoretically, this substance would be completely burned up if the body is in a normal metabolic state. The utilization of the usual amount of ingested carbohydrate is ample to oxidize completely this fatty acid before it can be excreted by the kidneys." Braasch demonstrated, however, that the introduction of beta-oxybutyric acid with a p_H of 4 into an infected bladder produced negative cultures in the majority of cases, thus demonstrating clinically the bactericidal action of the product.

M. L. Rosenheim,[7] of the University College Hospital, London, found the next piece to the jigsaw puzzle. The possibility suggested itself that a keto acid or hydrox acid might be found that would combine effective bacteriostatic power with resistance to oxidation in the body. Such an acid, if excreted unchanged in the urine and if nontoxic, should be able to replace the ketogenic diet. A number of fatty acids suggested themselves but were found unsatisfactory. Mandelic acid, an aromatic acid, was shown in 1863 by Shotten to be completely unaltered in the urine following administration to a dog. Experiments carried out on a dog substantiated this report and large doses proved nontoxic. A preliminary report of the clinical application of mandelic acid appeared in the London *Lancet* of May 4, 1935. On this favorable report, we obtained mandelic acid.[8] We are now reporting our clinical experience with fifty cases of pyuria treated by mandelic acid, as prescribed by Rosenheim.

The results obtained indicate that there is a definite value in the drug, superior to all other forms of medication in urinary infections. In a surprisingly large number of cases in which a highly acid urine was obtained, the results were most gratifying. Most of the failures could be readily explained.

Patients with suprapubic tubes, retention catheters, sinuses, and so on, were improved but were not made bacteria and pus free. Cases of alkali-encrusted cystitis failed to yield because of the persistent alkaline urine. The condition of patients with retarded flow of urine, such as pyonephrotic kidneys and hydro-ureters, improved wonderfully with the administration of mandelic acid. In the preoperative prostatic cases the results were favorable but not always completely effective. Those cases in which a p_H 5 was obtained cleared up promptly in most instances. Postoperative transurethral cases have responded favorably but much more slowly than cases of pyelitis.

Apparently the drug is most effective against the colon bacillus and less effective against the staphylococcus, Bacillus proteus and Bacillus pyocyaneus. Recurrence of pus and bacteria, after discontinuance of the medicine, occurred in some instances but yielded again promptly when again administered. Those negative to culture are more likely to remain so than those negative only to pus. In no instance have we noted any toxic effect or impairment of function during the use of the drug.

The treatment has been conducted in the following way: The urine was examined microscopically to determine the amount of pus and the morphologic appearance of the infecting organism. Cultures of urine aseptically collected by catheterization were made prior to and following treatment: The acidity of the urine was determined by nitrazine paper (Squibb) and nitrazine colorimeter charts, which offer a very simple and clinically satisfactory method. The patient was immediately placed on an acid-ash diet and given two ammonium chloride tablets, 0.5 Gm., four times daily. The acidity of the urine was tested daily and when a p_H of 5.5 or better was attained, which usually occurred in twenty-four hours, mandelic acid was prescribed in the following formula: mandelic acid 48 Gm., sodium bicarbonate 25.6 Gm., distilled water 480 Gm. A flavoring syrup to satisfy personal preference was added. In some cases nausea, diarrhea or dysuria occurred. This we considered to be due to the ammonium chloride rather than to the mandelic acid, since in changing to sodium biphosphate the mandelic acid could be continued. Wherever an alkaline condition persisted, a careful recheck of the food taken often disclosed the inclusion of orange or lemon juice, spinach, beans, molasses or olives in the diet. When these were removed and the acidifying agent increased, the proper p_H was established. The medication was continued in most cases for a week following the finding of a negative urine. If a recurrence developed the regimen was repeated.

Rosenheim, in a personal communication, states that he has been using the ammonium mandelate recently, which makes the urine acid without the necessity of using ammonium chloride. However, sodium mandelate

TABLE 1.—*B. Coli Infections*

Case	Days of Treatment	p_H of Urine	At End of Treatment: Culture	At End of Treatment: Microscopic Appearance	Diagnosis
1	9	4.5	Sterile	Negative	Chronic pyelitis
2	6	5.0	Sterile	Negative	Postoperative prostatectomy
3	4	4.5	Sterile	Negative	Acute cystitis
4	9	5.0	Sterile	Negative	Chronic cystitis; prostatic hypertrophy
5	11	4.5	Sterile	Negative	Nephrolithiasis and ptosis of right kidney
6	5	4.5	Sterile	Negative	Chronic pyelitis
7	5	5.5	Sterile	Negative	Cystitis; diverticula
8	9	4.5	Sterile	Negative	Postoperative prostatectomy, cystitis
9	9	5.0	Not sterile	Negative	Chronic pyelitis; hypertrophy of prostate
10	20	5.0	Unidentified rod	Negative	Pyelitis
12	7	5.0	Sterile	Negative	Acute cystitis
13	14	4.5	Not sterile	Negative	Hypertrophy of prostate; 10 oz. residual
14	7	5.0	Sterile	Negative	Chronic pyelitis
17	9	4.5	Not sterile	Negative	Chronic cystitis
18	7	4.5	Sterile	Negative	Acute cystitis
19	8	4.5	Sterile	Negative	Chronic pyelitis
22	14	5.0	Not sterile	Negative	Chronic pyelitis
26	19	4.5	Not sterile	Negative	Chronic cystitis, postoperative resection
27	6	5.5	Sterile	Negative	Chronic pyelitis
32	3	4.5	Sterile	Negative	Chronic pyelitis
33	3	4.5	Sterile	Negative	Hydronephrosis
34	5	4.5	Sterile	Negative	Vesical diverticula
35	12	4.5	Sterile	Negative	Pyonephrosis, kinked ureter
36	6	5.5	Sterile	Negative	Acute pyelonephritis
37	3	5.0	Sterile	Negative	Pyelitis, left kidney
38	6	5.0	Sterile	Negative	Pyelitis
40	9	5.5	Sterile	Negative	Pyelitis
41	9	5.0	Sterile	Negative	Hypertrophy of prostate, urinary retention
42	11	5.0	Sterile	Negative	Pyelonephritis
43*	5	5.5	Strep. viridans	Improved	Bilateral pyelonephritis, B. coli and Strep. viridans
44	6	4.5	Negative	Negative	Chronic cystitis, stricture
45†	7	4.5	Negative	Negative	Pyelitis
46	24	4.5	Not sterile	Negative	Postoperative prostatic resection
47	18	7.0	Not sterile	Improved	Multiple diverticula, stricture
48	4	5.0	Sterile	Negative	Pyelitis
49	10	4.5	Sterile	Negative	Pyonephrosis, right
50	2	5.0	Sterile	Negative	Chronic cystitis

* Patient died of Streptococcus viridans septicemia.
† Five years of age.

6. Cook, E. N., and Braasch, W. F.: Further Studies on the Use of Ketogenic Diet for Bacilluria, J. Urol. **33**: 583 (June) 1935.
7. Rosenheim, M. L.: Mandelic Acid in the Treatment of Urinary Infection, Lancet **1**: 1032-1037 (May 4) 1935.
8. The entire material has been supplied by the Mallinckrodt Chemical Company, St. Louis, through the Johannes-Tate Pharmacy.

and ammonium mandelate are quite hydroscopic and decompose. This is particularly true of ammonium mandelate. The mandelic acid is quite stable and the most convenient form for the druggist.

The results obtained in some cases of chronic pyuria have been remarkable. Cloudy urine that has resisted all forms of medication has become crystal clear in four or five days. A brief citation of a few will convey the favorable impression which we have received with its use.

Mr. J. S. S. of Cairo, Ill., had a suprapubic prostatectomy performed in 1926 and always thereafter had pus in the urine provoking episodes of epididymitis or outbreaks of other urinary infection. All forms of urinary antiseptics and dilations failed to clear the urine. Mandelic acid was administered and in four days the urine was grossly and culturally negative.

TABLE 2.—*B. Proteus Infection*

Case	Days of Treatment	p_H of Urine	At End of Treatment: Culture	At End of Treatment: Microscopic Appearance	Diagnosis
23	25	Alk.	Not sterile	Not improved	Chronic cystitis
24	21	4.5	Not sterile	Not improved	Chronic cystitis
29	10	5.5	Not sterile	Not improved	Chronic pyelitis, prostatic hypertrophy
30	13	4.5	Not sterile	Not improved	Chronic cystitis following removal of bladder stones
31	15	5.0	Not sterile	Improved	Chronic cystitis, postoperative prostatectomy
39	6	5.0	Sterile	Negative	Pyelitis, B. proteus

Mrs. W. G. C., aged 69, came from Washington, D. C., for treatment of a chronic cystitis and trigonitis. Undernourished, hampered with sinusitis and chronic bronchitis, she resisted all efforts to stamp out this persistent pyuria. In five days after the administration of mandelic acid, the urine became clear and urinary symptoms improved. The urine, cultures of which five days previously yielded B. coli in abundance, was found normal and the patient returned home within ten days.

In March 1934 we performed a right nephropexy on Mrs. E. B., of East St. Louis, Ill., which relieved her attacks of right renal colic, but later she became afflicted with a left pyelitis and cystitis, which persisted unrelentingly with symptoms of frequency, urgency, and bearing down perineal pain. Her teeth were examined and treated, the tonsils removed and various shock medications, including typhoid serum and neoarsphenamine, administered, but the symptoms persisted. The urine from the left kidney showed pus 2 plus, B. coli 3 plus. She was given ammonium chloride and mandelic acid and within four days the urine was clear of pus and bacteria, with a p_H of 4.5 and alleviation of symptoms.

Mr. R. S. D., aged 38, had bilateral pyonephrosis with right renal calculi and persistent pyuria since first seen in 1932; the organism was B. coli. Since each kidney had a retention of about 20 cc., this case offered a good example of what effect the medication would have on a retarded flow of urine. The mandelic acid was started June 30, and on July 13 the urine was clear and negative to culture. The patient states that he feels much better and does not tire as easily. The urine was still clear one month after treatment.

Mr. B. F. E., aged 62, had hypertrophy of the prostate gland, causing 2½ ounces (75 cc.) of residual urine. The patient was first seen June 26, 1936, when the urine was alkaline with pus 2 plus and B. coli 3 plus, the culture showing numerous colonies of B. coli. The temperature ranged up to 101 F. Medication was started the same day. Five days later the temperature was normal, the urine showing only an occasional pus cell although the culture still showed colonies of B. coli. A transurethral prostatectomy was performed on July 2 and the mandelic acid resumed the next day. The catheter was removed the third day and the patient completely emptied his bladder, voiding very cloudy urine. August 12, however, the urine was clear. The laboratory reported the p_H 4.5, no pus, no bacteria and culture negative. Never before have we experienced such an early clearing up of urine following transurethral work.

The acute cases of pyelitis and cystitis are affected very promptly, as shown by the following:

Miss M. M., aged 22, complained of frequency and pain on urination, with urgency and pain in the left renal region. The day of the administration of the drug, July 12, the urine was acid, with a p_H of 5.0. The pus was 3 plus, the micro-organism B. coli 2 plus, and red blood cells 1 plus. July 15, three days later, the urine was clear with no pus or bacteria microscopically examined and the culture was negative. She was dismissed July 19 with relief from all symptoms.

An analysis of the accompanying tables shows thirty-seven cases of Bacillus coli infection, embracing acute and chronic pyelitis, pyelonephritis, vesical diverticula, nephroptosis, renal calculus, prostatic hypertrophy with retention and cystitis. All these became microscopically clear under the treatment. Seven yielded positive cultures.

The average number of days of treatment required to produce negative urines was 7.1. The seven cases of coccic infections, although improved, were not made sterile. This group is too small to conclude definitely that this organism is altogether resistant, especially when they are reported as being affected in vitro.

Of the six cases of Bacillus proteus infection, only one was made sterile. The proteus organism, we find, is most resistant in the urinary tract. Eighty-one per cent of all colon infections treated resulted in sterile cultures. Practically all cases improved symptomatically and the urines became less cloudy. We conclude from this survey that a urinary infection of a colon bacillus type, in which a p_H of 5.5 is obtained, may be expected to clear up with the administration of mandelic acid within four to twelve days.

It is highly important to emphasize that all these patients were subjected to careful urologic study and the original causative factor in producing the pyuria was recognized and treated in the realization that the pyuria was only one manifestation of the trouble. The real value of the drug will be lost and actually be prejudiced if it is indiscriminately used before the diagnosis is made. Pyuria is only a "physical symptom" such as fever, and any physician who is content to give relief only temporarily is a questionable practitioner. Because of the apparent effectiveness of mandelic acid in inhibiting the growth of B. coli, this report should in no way be construed as indicating it as a panacea for all urinary ills; but we wish to show by the case reports that pyuria is the end product of many com-

TABLE 3.—*Staphylococcic Infections*

Case	Days of Treatment	p_H of Urine	At End of Treatment: Culture	At End of Treatment: Microscopic Appearance	Diagnosis
11	17	6.0	Not sterile	Improved	Postoperative transurethral resection
16	9	6.5	Not sterile	Not improved	Bilateral nephrolithiasis
20	15	Alk.	Not sterile	Not improved	Alkaline incrustations
21	23	4.5	Sterile	Not improved	Pelvic vesical sinus
25	15	5.0	Not sterile	Improved	Chronic cystitis, postoperative prostatectomy
28	13	5.5	Not sterile	Improved	Nephrolithiasis
			Unclassified		
15	12	5.5	Strep., coli	Improved	Cancer of prostate

plicated diseases the cure of which calls for more than the administration of mandelic acid by mouth. Manifestly renal stone, kinked ureter due to movable kidney, prostatic hypertrophy, bladder diverticula, and stricture of the ureter or urethra—all found in the group studied—required more than the administration of mandelic acid; but mandelic acid was found most helpful in decreasing operative risk, where indicated, making the patient more comfortable and shortening the length of illness.

It is evident from the report of Dr. Anson Clark, who performed experimental work on dogs, that caution should be exercised in giving the proper dose and in cases of lowered renal function.

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MANDELIC ACID IN THE TREATMENT OF INFECTIONS OF THE URINARY TRACT

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In recent years the treatment of infections of the urinary tract has taken on a more scientific aspect. The older empirical methods which were efficacious in alleviating symptoms have been supplanted by newer forms of treatment which have a logical and predetermined basis and the value of which has been proved.

Since Shohl and Janney [1] demonstrated that the growth of Escherichia coli was inhibited in urine at a p_H of 4.6 to 5.0, the question of combating infection of the urine has come steadily to the foreground. Clark [2] in 1931, searching for a means of acidifying the urine, used the ketogenic diet. Early observations soon revealed that a secondary factor was needed besides high acidity if bacillary infections of the urinary tract were to be eradicated. Fuller [3] proved this secondary factor to be beta-hydroxybutyric acid. Helmholz and Osterberg [4] have definitely shown that a certain concentration of this acid, which is an end product of the ketogenic diet, is needed along with a certain p_H of urine if negative cultures of urine are to be obtained.

As the ketogenic diet requires the most careful and skilful management if good results are to be obtained,[5] and as it often causes distressing general and gastrointestinal symptoms, a vigorous search has been going on for a simpler and more easily managed means of treatment which would obtain the same results. When beta-hydroxybutyric acid is given by mouth to patients on a normal diet, it is oxidized in the body to carbon dioxide and water. Rosenheim,[6] after experimenting with similar organic acids, found that mandelic acid could be given by mouth and could be recovered in the urine unchanged. Helmholz and Osterberg [7] carried on a series of experiments in the laboratory and demonstrated very definitely that the usual bacilli found in the urinary tract were definitely killed by a 0.5 per cent solution of mandelic acid at a p_H of 5.5. As with beta-hydroxybutyric acid, a lower p_H will not require such a high concentration of the acid.

During the past twelve months we have been using mandelic acid or its derivatives with varying results. Our earlier work revealed its efficacy in approximately 50 per cent of cases, but later experience has shown that, with more careful management, better results may be obtained. We have given a 10 per cent solution of sodium mandelate, the dose being 1 ounce (30 cc.) before meals and at bedtime. On this regimen the patient ingests 12 Gm. of the drug daily. In order to render the urine acid, either ammonium nitrate or ammonium chloride was given in doses of from 4 to 6 Gm. each day. Patients were instructed to take only five glasses of fluid daily in order not to dilute the urine. The results obtained were as follows: Seventy-five patients were given the drug, and the urine of sixty-one of them, or 81 per cent, was rendered sterile.

In an attempt to obtain the desired acidity of the urine without using an additional acidifying drug, Holling and Platt [8] suggested the use of the ammonium salt of mandelic acid and reported good results in four cases. In one of these cases they found that the addition of ammonium chloride was required to obtain a satisfactory p_H. We have given a 10 per cent solution of the ammonium salt of mandelic acid to five patients, and in all but one case a satisfactory p_H was obtained without the addition of an acidifying drug. Another salt of mandelic acid is ethanolamine mandelate, and this too is designed to eliminate the use of a secondary drug. Ethanolamine mandelate was given to five patients, and negative cultures were obtained in three of these cases. In one case an acidifying drug had to be added.

Recently the ammonium salt of mandelic acid has been prepared in a 40 per cent syrup solution, and this has proved very efficacious. It was given to twelve patients with bacillary infections of the urinary tract, and in eleven of the cases the urine was sterilized. One patient required ammonium nitrate to bring about the desired acidity of the urine.

Offhand this form of therapy may seem extremely simple. The physician can write a prescription for mandelic acid and an acidifying drug and the cure is assured. This is not actually the case, however, and unless the physician is alert in his management of these patients and checks the p_H of the urine daily, he will be greatly disappointed in the results he obtains.

In using the ketogenic diet, the diet itself aids greatly in acidifying the urine; with mandelic acid therapy this factor is lacking, and, if the mandelate plus the acidifying drug will not bring about a high acidity, other means must be instituted. In a few cases hydrochloric acid by mouth has been sufficient to increase acidity; in other cases an acid-ash diet has been tried, with varying results, and in still other cases the addition of the ketogenic diet has been necessary before the p_H was low enough and bactericidal urine was obtained.

From the Section on Urology, the Mayo Clinic.

1. Shohl, A. T., and Janney, J. H.: The Growth of Bacillus Coli in Urine at Varying Hydrogen Ion Concentrations, J. Urol. **1**: 211-228 (April) 1917.
2. Clark, A. L.: Escherichia Coli Bacilluria Under Ketogenic Treatment, Proc. Staff Meet., Mayo Clin. **6**: 605-608 (Oct. 14) 1931.
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4. Helmholz, H. F., and Osterberg, A. E.: The Concentration of Beta-Oxybutyric Acid and the p_H in Bactericidal Urine, Proc. Staff Meet., Mayo Clin. **9**: 46-48 (Jan. 17) 1934.
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6. Rosenheim, M. L.: Mandelic Acid in the Treatment of Urinary Infections, Lancet **1**: 1032-1037 (May 4) 1935.
7. Helmholz, H. F., and Osterberg, A. E.: The Rate of Excretion and Bactericidal Power of Mandelic Acid in the Urine, Proc. Staff Meet., Mayo Clin. **11**: 373-377 (June 10) 1936.
8. Holling, H. E., and Platt, Robert: Mandelic Acid and Ammonium Mandelate in the Treatment of Urinary Infections, Lancet **1**: 769-771 (April 4) 1936.

While mandelic acid therapy may supplant treatment with the ketogenic diet in approximately 75 per cent of the cases, it cannot replace it entirely. We believe the main reason for this is the question of maintaining high acidity of the urine, as discussed in the previous paragraph. In conjunction with the ketogenic diet, mandelic acid will be extremely helpful. Often with the diet alone we were able to gain satisfactory acidity, but the concentration of beta-hydroxybutyric acid was not great enough to render the urine bactericidal. The addition of mandelic acid salts in this group of cases has already proved of great value. In one case in which diabetes insipidus was present as well as a urinary tract infection and the patient was on the ketogenic diet, extreme dilution of the urine prevented a sufficient concentration of beta-hydroxybutyric acid to obtain the desired results. The addition of sodium mandelate while the patient was still taking the diet sterilized the urine. Here, either form of therapy alone would have failed but the two used together were highly successful.

The urologic indications for the use of mandelic acid are the same as those for use of the ketogenic diet. To date, bacillary infections are readily attacked with this form of therapy while coccic infections are not.

As with the ketogenic diet, treatment of bacilluria associated with stone, stasis or marked prostatitis will be more difficult and will require the same thoroughness. The contraindications to the use of mandelic acid are also similar to the contraindications to the use of the ketogenic diet. However, in certain cases in which patients have gout, gastric or duodenal ulcer, or diabetes mellitus, when the use of the ketogenic diet is impossible, we believe that mandelic acid will be extremely beneficial and cause no distressing results. Helmholz and Osterberg have already shown in studies on animals that excessive doses of the drug will destroy the renal function and even produce death. In a series of normal individuals who were given the drug to determine the normal rates of excretion, determination of urea in the blood and of phenolsulfonphthalein excretion in the urine were made before the patients took the drug and after a week's ingestion of 12 Gm. daily. At the end of the week the blood urea was found to be increased in all cases; the percentage of excretion of phenolsulfonphthalein was decreased. Whether or not this apparent decrease in renal function is attendant on a lowered intake of fluid or can be attributed to the drug itself we cannot say, but certainly we feel that one should be cautious in using the drug for patients who already have a reduced renal function and, particularly, for the aged. Further studies along these lines are now being conducted, and until experience with the use of this drug is greater, it must be used with care.

Most of our patients have taken mandelic acid or its derivatives without any untoward effects, less than 1 per cent having experienced any nausea or vomiting. Approximately one in ten have noticed some diarrhea, but in most of these cases it was of a mild character; a few patients, however, did have from eight to fourteen stools a day and administration of the drug had to be stopped for a while. Its administration was resumed again later in decreased dosage without producing any ill effects.

In conclusion, we again wish to call attention to the importance of close observation and careful management of patients being treated with mandelic acid if the desired results are to be obtained.

EXPERIENCES WITH AMMONIUM MANDELATE IN URINARY INFECTIONS

A REPORT OF RESULTS OBTAINED IN SIXTEEN CASES OF VARIOUS TYPES OF INFECTIONS REGARDLESS OF THE EXISTING PATHOLOGIC CONDITION

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The medical profession is occasionally presented with a new urinary antiseptic before sufficient time has elapsed to permit competent observers to test adequately its therapeutic results. For that reason some drugs are used indiscriminately in all types of urinary infection instead of being restricted to the specific infections for which they were originally intended. Through this practice they sometimes fall into disrepute because of seemingly poor results.

At the present time we are apparently on the threshold of another such possibility. Recently some well known research workers through a logical sequence of events and experiments have presented the medical profession with an oral medication that has given startling results in certain types of urinary infection. Yet it has not been sufficiently investigated by controlled clinical and laboratory study to warrant its general distribution and use under the unrestricted title of "urinary antiseptic." Such a general term will undoubtedly bring it into early disrepute because of failure in some cases even if it should not cause untoward results and complications.

Clark and Helmholz [1] in October 1931 called attention to the value of ketogenic treatment in various urinary infections, and the Nesbit [2] modification of the ketogenic diet is well known. It is this modification that I have followed as a routine because of its greater simplicity and likewise because it is better tolerated. Although the ketogenic diet has given remarkable results in bacillary infection of the urinary tract, it is not entirely satisfactory because of the strict regimen and the nauseating ingredients. This often causes the patient to become lax in its routine and necessitates hospitalization in most cases. It then becomes an economic problem in order to obtain the desired results.

Just as the discovering of the bacteriostatic properties of beta-hydroxybutyric acid led to the use of the ketogenic diet in urinary infections,[3] so Rosenheim [4] and others followed through in their investigations to produce a like condition in the urine as that which resulted from the use of the ketogenic diet. It was known by these men that beta-hydroxybutyric acid could not be used by oral administration because it was metabolized by the body. The use of other organic acids in the treatment of urinary infections was tried without effect. Then Rosenheim reported that mandelic acid passed through the body unchanged. When excreted in sufficient concentration in a urine with an acidity below a p_H of 5.3, it was sufficiently bacteriostatic to be of practical value and comparable to the use of the ketogenic diet.

Read before the Detroit Branch of the American Urological Association at Ann Arbor, Mich., Oct. 24, 1936.

1. Clark, A. L., and Helmholz, H. F.: Proc. Staff Meet., Mayo Clin. **6**: 605 (Oct. 14) 1931.
2. Nesbit, R. M.: Urologist's Correspondence Club Letters **2**, Aug. 7, 1935.
3. Fuller, A. T.: Lancet **1**: 855 (April 22) 1933.
4. Rosenheim, M. L.: Lancet **1**: 1032-1037 (May 4) 1935.

Later in December 1935, Lyon and Dunlop [5] confirmed these observations and called attention to the use of mandelic acid salts.

In April 1936, Holling and Platt [6] reported twenty-nine cases treated with mandelic acid salts and suggested the use of the ammonium salts as preferable. Previously in the use of mandelic acid as such, sodium bicarbonate was given as a neutralizing agent or buffer. This in turn required the administration of ammonium nitrate or ammonium chloride in order to maintain the acidity of the urine below a p_H of 5.3, or the degree necessary to produce the best results. This combination often caused considerable gastric distress, nausea and sometimes vomiting of the drug.

In July of this year, Cook of the Mayo Clinic, in a letter to the Urologist's Correspondence Club, reported the use of 40 per cent solution of ammonium mandelate in five cases of urinary infection. Negative cultures were obtained in all cases. These patients were given an alkali-free diet, and their fluid intake was limited to one liter daily. Interested by this report, we decided to try it. We were confronted, however, with the fact that such a drug was not available commercially in the United States, though it was available in England in the form of sodium mandelate. Through the cooperation of a local chemist mandelic acid was obtained, and from this he made up ammonium mandelate, but to make it more palatable a 40 per cent elixir was prepared. This preparation has been well tolerated by all our patients. At the present time several of the larger pharmaceutical houses either have mandelic acid preparations on the market or are preparing to announce them.

We have used ammonium mandelate in various types of urinary tract infections both in our office and in our hospital practice, and we offer a summary of the results obtained in sixteen cases which we have treated.

In using this treatment the patients are given 2 drachms of the 40 per cent elixir of ammonium mandelate, which amounts to 3 Gm. (7.5 cc.) of mandelic acid, four times daily in a small quantity of water. The total fluid intake in twenty-four hours should not exceed 1 liter of fluid, actually measured at the beginning of each twenty-four hours and evenly distributed to maintain a balanced concentration. The patient, if not hospitalized, is cautioned against the use of all other drugs, also foods and fruit juices, which might readily produce an alkaline urine. No other restrictions seem necessary. If the patient is not physically incapacitated he may carry on his usual occupation. We have maintained, however, a close check on each patient with a daily cell count of the urine and a p_H determination. This observation is obviously necessary for proper control of the case.

One of the fundamental principles in the treatment of urinary tract infections is the elimination of existing obstructive lesions and the establishment of free drainage. The first case in our series presented such a marked degree of renal ptosis and obstruction, as shown by the pyelogram, yet such striking results were obtained on ammonium mandelate therapy, that I will report it in detail. I am doing this so that other physicians also will be favorably impressed as my associates and I were, for this case offered us moral support in the face of failures encountered in some other types of infection.

5. Lyon, D. M., and Dunlop, D. M.: Brit. M. J. **2**: 1096 (Dec. 7) 1935.
6. Holling, H. E., and Platt, Robert: Lancet **1**: 769-771 (April 4) 1936.

REPORT OF CASES

CASE 1.—A white woman, aged 67, who was very emaciated and confined to her bed, was first seen on Aug. 4, 1936, because of pain in the region of the bladder and urethra, frequency of urination accompanied with burning, and pain in the back, particularly over the right lumbar region. These symptoms had been present with increasing intensity during the previous several months. Cystoscopic examination revealed the bladder urine to be turbid with pus. A large amount of grayish débris was hanging from the bladder walls, and the blood vessels of the bladder mucosa were markedly congested. On ureteral catheterization, clear urine was obtained from the left kidney while turbid urine containing approximately 200 pus cells per low power field was obtained from the right kidney. The cultures from the right kidney and bladder yielded colon bacilli. The left kidney culture was sterile. Pyelography demonstrated a normal left kidney and a large, hydronephrotic, ptosed right kidney. The ptosis was of such a character that the pelvis did not have free drainage from the position in which it reposed. More than 150 cc. of purulent urine was aspirated through the right ureteral catheter before the contrast medium

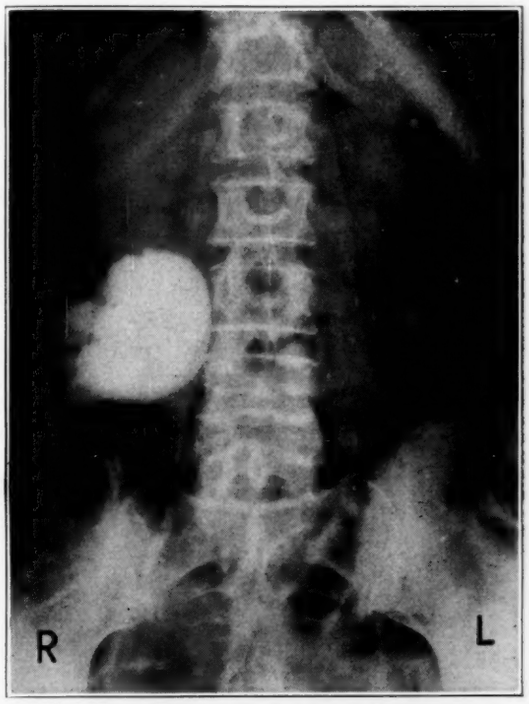

Fig. 1 (case 1).—Right pyelo-ureterogram showing marked dilatation and ptosis, and obstruction at the ureteropelvic junction.

was injected for pyelography. The ureteral catheter was fixed in place for drainage and pelvic lavage of the right kidney was carried out at frequent intervals over a period of several days. Various urinary antiseptics were given by mouth but this treatment proved valueless, for when the catheter was removed seven days later the symptoms recurred. An intravenous urogram August 12 showed the right kidney to have fair function but no change in the hydronephrosis. Nephrostomy, nephropexy and nephrectomy were considered but, owing to the poor general condition of the patient and her aversion to surgery, we decided to try the ammonium mandelate therapy first. The treatment was started August 24 at which time the urine contained from 15 to 20 pus cells per high power field, uncentrifugated urine. August 26 a voided specimen showed 8 to 10 pus cells per high powered field. September 1 the cell count was about the same, with some granular casts being present. September 10, sixteen days after starting the therapy, 2 pus cells per high power field were found. The urinary symptoms had disappeared except for some burning on urination. The p_H of the urine had varied from 4.5 to 5.3 throughout the treatment. September 15, twenty-one days after the medication was started, there were but slight urinary symptoms and the general condition was improved. The remarkable absence of pus in the

bladder urine made us skeptical of a possible painless blocking of the right ureter. We therefore catheterized the right kidney and found no pus in the urine from this side and a sterile culture was obtained. Examination of the urethra showed it to be inflamed and edematous, this apparently being the cause of the burning on urination. For the last month the patient has been up and around her home without pain or symptom and the urine is still free of pus.

Case 2.—As the results in our first case were so striking and were evident so early in the treatment, we felt that we might try it in a mixed type of infection. An elderly, prostatic patient two years previously had suffered an apoplectic attack, which confined him to his bed with a right sided paralysis, difficult speech and acute retention of urine. At the time we saw him, during the early days of his paralysis, the urine was purulent and a retention catheter was fixed in place. After prolonged hospitalization, the patient was able to be up and about, unassisted. The urine, however, remained turbid with infection and he was under constant treatment of bladder irrigations and oral urinary antiseptics. His prostate was markedly enlarged. It was smooth, firm and not sensitive. No nodules were palpable. Cystoscopic examination showed the

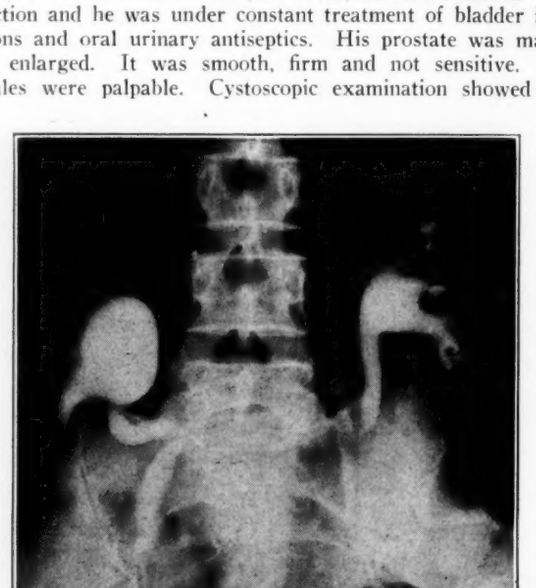

Fig. 2 (case 15).—Upright pyelo-ureterogram (retrograde) showing ptosis and obstruction with dilatation of right kidney pelvis and ureter.

blood vessels of the bladder to be congested and the bladder walls trabeculated. There was a massive intravesical encroachment of both lateral lobes of the prostate. Because of the patient's general condition we had advised against operative procedure. Aug. 31, 1936, we started this patient on ammonium mandelate therapy, at which time the urine contained 150 pus cells per high power field and the culture of the urine yielded staphylococci. September 2 the amount of pus had not changed. September 8 the pus had decreased to from 50 to 60 pus cells per high power field but there was present also some 60 to 75 red blood cells. The patient also was complaining of considerable gastric distress and loss of appetite. It was learned that he was taking the ammonium mandelate undiluted, which may have accounted for the severe gastric distress; but it would not account for the blood cells in the urine. The p_H value was maintained at 5.5 or below. September 10 the condition was better. The urine contained around 40 to 50 pus cells and about the same number of red blood cells per high power field. September 13, two weeks after treatment was started, the patient had taken 16 ounces (475 cc.) of the elixir of ammonium mandelate. A check of the urine showed 150 pus cells present per high power field. There was an occasional red blood cell present. This was thirty-six hours after the medication had been stopped, and the p_H of the urine had risen to 6.0. The following day the patient had an acute retention of urine and in general had lost ground in physical strength throughout the course of the treatment. Several days of palliative treatment were given. A retention catheter was used, but the patient was unable to tolerate it and a cystostomy was done for relief. A transurethral resection is now contemplated, since suprapubic drainage is established. This patient, we feel, was not benefited by the treatment and complications were encountered.

Case 3.—A white man, aged 72, was first seen Jan. 22, 1936, because of urinary obstruction, which had been present in an increasing degree for the past ten years. During the previous three months occasional attacks of hematuria occurred. Rectal and cystoscopic examination revealed a large prostate, grade 3 in size, with an 8 ounce (235 cc.) residual urine. Many small stones were present in the bladder and marked edema of the floor was present also. A two stage suprapubic prostatectomy was performed. Convalescence was slow but uneventful. He left the hospital seven weeks after admission and returned to the office for further treatment. His condition improved rapidly. He voided freely; nocturia disappeared. He regained his weight and strength and returned to his work. There were no symptoms of any type and no residual urine, yet in spite of bladder irrigations and prolonged use of various urinary antiseptics the urine remained turbid with pus and colon bacilli. There have been no symptoms of kidney infection at any time. An x-ray film of the kidney, ureter and bladder was negative for stone shadows. Ammonium mandelate therapy was started August 22, at which time the urine contained colon bacilli and from 25 to 30 pus cells per high power field and a p_H of 7.0. August 24, two days after treatment was started, the pus had decreased to an average of 18 cells per high power field. September 1 it was reduced to from 2 to 4 cells per high power field. September 9, two days after the treatment had been stopped, it contained from 8 to 12 pus cells per high power field and, on staining, various types of bacteria were found. Through the course of treatment the p_H remained at 5.0, while a few days after treatment was stopped the p_H rose to 7.5. This is a case which was undoubtedly aided by the mandelic acid therapy. The colon bacilli were eliminated while other organisms appeared later. This patient lives 50 miles from the city and it is difficult to maintain him on a routine which we desire, but I believe that, if this patient is placed on treatment under different circumstances for a sufficient period, his condition will be greatly improved.

Case 4.—A white woman, aged 27, was first seen Aug. 1, 1936, on account of pain in the right kidney region, which was intermittent in character. These symptoms had been present for two years but had not been severe until three months previously. Cystoscopy and pyelography at this time showed a normal bladder with a moderately dilated right kidney pelvis, the condition apparently being due to a constriction at the ureteropelvic junction. Urine specimens from the kidney produced negative cultures, and an upright pyelo-ureterogram showed no ptosis of the kidney. Following the examination, the patient's symptoms were greatly aggravated. There was an elevation of temperature, and pus and blood appeared in the urine. We felt that we had introduced an infection into a partially blocked kidney. She was kept at bed rest on urinary antiseptics and forced fluids. After a period of two weeks when she was feeling better we dilated the right ureter to a size 14 F. Urine obtained from the left kidney at this time was negative, while the right side showed pus and staphylococci. After this dilation there was again an aggravation of symptoms, which subsided after a few days of bed rest and urinary sedatives, but the original symptoms persisted. We started giving ammonium mandelate August 29, at which time a specimen of urine showed a p_H value of 6.0 and contained from 4 to 6 pus cells per high power field. The culture yielded staphylococci. During treatment the p_H varied from 4.5 to 5.5. The number of pus cells ranged from 2 to 8 per high power field. After two weeks of ammonium mandelate therapy the urinary examination gave approximately the same results as the day on which it was started. In this case I feel that the therapy was of no value. After the therapy was stopped, the patient's general condition improved under forced fluids and an increased diet. This was followed by a gradual diminution of pus in the urine.

Case 5.—This case is of interest because of its long standing history. A man, aged 61, was first seen in 1932 because of

hematuria and pyuria and symptoms of obstructive urination. These symptoms had been present at intermittent intervals over a period of several years. Cystoscopy and cystography in 1932 revealed a large intravesical prostate, marked trabeculization of the bladder with multiple small diverticula, and one large diverticulum which was practically the size of the bladder. Prostatectomy and diverticulectomy were subsequently done and the patient had a prolonged convalescence. For many weeks after leaving the hospital he was treated with bladder irrigations and urinary antiseptics but the urine persisted to be turbid. Cystoscopy revealed the large diverticulum to be absent, but the smaller ones remained about the same size. Though the patient remained well for the intervening time from 1933 to the present, the urine never changed in character. Sept. 15, 1936, he returned to the office for routine examination and it was decided to try him on ammonium mandelate. Culture of the urine showed gram-positive bacilli and diplobacilli. The p_H before the treatment was started was 7.0. Two days after it was started the urine was clearer than at any time in many years of the patient's memory. The p_H was 4.5 and there were from 4 to 6 pus cells per high power field. The patient continued on the treatment for only twelve days, as his business required a long absence from the city. Throughout his treatment the p_H value of the urine varied from 4.5 to 5.0. At the time of the discontinuance of the treatment the urine still contained an occasional pus cell per high power field and some bacteria were still present in a smear. This case I feel will probably go on to a possible cure when the patient returns for further treatment.

CASE 6.—The sixth case is of interest because the culture of the urine before the therapy was started contained diplococci and streptococci. A man, aged 61, was seen because of symptoms of urinary obstruction. A transurethral resection of the prostate was done June 30, 1936. He made an uneventful recovery from this. There was no residual urine. He had frequency of urination of three to four times a day and nocturia from one to two times, when seen September 19. The urine remained turbid in spite of frequent bladder lavage and oral urinary antiseptics. The p_H of the urine was 7.0. He was started on ammonium mandelate on this date and two days later, September 21, the urine appeared clear. There was an average of only one pus cell per high power field, and the p_H was 5.0. As the patient was complaining of loss of weight while on treatment and because of the apparent cure, I felt justified in stopping the therapy at this time. Five days later, however, he returned to the office and the urine was again hazy with pus and bacteria. The p_H was 6.0. Ammonium mandelate was resumed, and October 10 the urine was clear with a p_H of 5.0 and there was an average of about 1 pus cell to every two or three high power fields. October 14 the urine was sterile, but the treatment was continued for five more days. This made a total in this case of 6 ounces (180 cc.) of 40 per cent ammonium mandelate in the first course of treatment and 16 ounces (475 cc.) in the second and last series. October 22, two days after discontinuance of the drug, the patient returned to the office with a slightly hazy urine containing many bacteria and a rare pus cell. Cultures taken at this time have not yet been reported. This infection seems to show marked resistance to the treatment. At least recurrence appeared soon after the treatment was stopped. I believe that better results could be obtained in this case with the use of additional ammonium chloride to maintain the p_H around 4.5.

CASE 7.—A man, aged 49, seen first Oct. 2, 1936, with symptoms of acute cystitis, was hospitalized and on October 5 urologic study revealed a marked cystitis suggestive of tuberculosis. Pyelography showed slight irregularity in the minor calices of the left kidney similar to that sometimes seen in early tuberculosis. Urinalysis demonstrated many pus cells from both kidneys. Culture of the left kidney yielded staphylococci and of the right kidney diplobacilli. No tubercle bacilli were found in smears. Guinea-pigs were inoculated with separate urine specimens. The patient was placed on ammonium mandelate therapy and allowed to return to his home in another city under the supervision of his local physician. One week later the physician reported all symptoms worse and hematuria present. The therapy was discontinued and palliative measures were instituted. Seventeen days later the guinea-pigs are still alive, but not ready for autopsy; still I feel that, clinically this is probably a case of renal tuberculosis. The irritability of the urinary tract on acid treatment seems to substantiate this diagnosis.

CASE 8.—A man, aged 75 on whom a prostatic resection was done in August 1935, had a resulting residual pyuria of 20 cc. Routine treatment did not change this condition nor did the absence of treatment alter the urine. September 24 he was first given ammonium mandelate, when culture showed Bacillus coli present. October 19 the culture was sterile and the urine was hazy with red blood cells, which averaged 8 per high power field. Treatment was discontinued. This patient was on treatment twenty-five days. The blood appeared the last three days. The prolonged treatment was probably due to the fact that the p_H remained above 6.0 during the first eight days. He admitted that during the first week he was taking more than the prescribed amount of fluid.

CASE 9.—This is a case of hypertrophied prostate and diverticulum in a man, aged 71. The prostate was resected July 14, 1936, in the face of a diverticulum with a capacity of approximately 60 cc. The patient made an uneventful recovery except for the remaining pyuria, which was unaffected by treatment.

Fig. 3 (case 16).—Pyelogram showing marked dilatation and ptosis of right kidney.

Bacillus coli appeared in cultures from the urine October 2, and the patient was started on ammonium mandelate. Five days later the urine was clear with 1 or 2 pus cells being present per high power field. On the tenth day cultures were sterile, but from past experience treatment was continued for three more days and the patient now is on observation apparently cured, though nothing was done to the diverticulum, which was located on the floor of the bladder.

CASE 10.—This case is interesting because of the differential diagnosis. The patient was sent into the hospital by a gynecologist because of pain in the right lower quadrant and pus in the urine. He was satisfied that the right adnexa were normal. She had an appendectomy two years previously. On admission to the hospital a catheterized specimen of bladder urine was obtained and a large amount of pus was found; likewise the culture showed diplococci and diplobacilli. The patient was started on ammonium mandelate without further examination. Thirty-six hours later, as the pain still persisted and the temperature remained at 102 F., where it had been on admission, we were stampeded into doing a ureteral catheterization. This was the first case of acute pyelitis in which we had used this therapy and we were willing to be stampeded. The catheterized

urine from the kidneys showed no pus and no cultural growth from the left side, while from 30 to 35 pus cells per low power field were obtained from the right kidney and the culture showed diplococci and diplobacilli. Against advice, we removed the catheters from the kidneys and continued the mandelic acid therapy. Two days later the temperature dropped to normal. The catheterized specimen of urine from the bladder showed from 1 to 2 pus cells per high power field and a p_H of 4.5. The following day the patient was allowed out of bed and on October 13, six days after the therapy was started, the patient was allowed to go home. A culture at that time was sterile. On October 22 the patient had no complaints, the temperature remained normal and the urine was free of pus.

Case 11.—A man, aged 72, entered the hospital suffering from pain in the right lumbar region radiating inferiorly and anteriorly. Examination revealed a calculus in the right renal pelvis, another in the right lower ureter near the ureterovesical juncture and two in the left lower ureter, and one in the bladder. Each was approximately the size of a small green pea. The patient also had a hypertrophied prostate with both vesical and urethral encroachment. The ureteral and bladder calculi were delivered by cystoscopic manipulation and a transurethral resection of the prostate was subsequently done. The patient left the hospital with a calculus still remaining in the right renal pelvis and a urine cloudy with pus and colon bacilli. This was in June 1936. Routine treatment did very little toward clearing the urine. Ammonium mandelate was first given October 14. Five days later the urine was clear and cultures were sterile.

Cases 12 and 13.—In these two cases we used the ammonium mandelate very closely following transurethral resection of the prostate. The first patient was a man, aged 81, and treatment was started ten days after operation while he remained in the hospital making a very slow recovery. The culture yielded staphylococci. The patient was on treatment six days without apparent change in the urine. Because of dehydration he was removed from this therapy.

The second case, in which therapy was started soon after resection of the prostate, gave a culture of Streptococcus viridans. Treatment was started three days after resection. Bladder irrigations were used in conjunction in both cases. On the fourth day of treatment, seven days after resection, improvement was noted but a secondary hemorrhage occurred which necessitated discontinuance of the treatment.

Case 14.—A hospital orderly, aged 25, had a known pyuria prior to a gonococcic infection with accompanying epididymitis. He had been in the hospital ten days when I first saw him. The gonorrheal infection was in a subacute stage and the epididymitis was subsiding. Voided specimens of urine were cloudy with pus. No cultures were made but the patient was put on mandelic therapy to see if it might give any clinical results. It did. After twenty-four hours of administration of ammonium mandelate, it was discontinued because of the onset of severe urethral irritation.

Case 15.—The next two cases are somewhat similar because they show the same pathologic type, which consists of a right sided pyelonephritis and ptosed, hydronephrotic right kidney. Both have purulent pus in the right kidney. These cases were seen on the same day. The first one, on cystoscopic examination, showed from 6 to 8 pus cells per low power field in the left kidney and about 700 or 800 per low power field in the right kidney. Both cultures yielded were colon bacilli. The pyelograms (figs. 2 and 3) reveal the type and degree of hydronephrosis and ptosis. Both cases evidently show stasis. Patient 15 entered the hospital for urologic study, after which she was started on ammonium mandelate October 1. Two days later she left the hospital and returned to the office, stating that she felt much better. The urine appeared to be much clearer in a voided specimen. The p_H was 5.5. October 5, five days after treatment was started, a catheterized specimen of urine was clear. There were from 2 to 3 pus cells per high power field. The p_H was 5.0. The patient stated that she had not felt as well in many weeks. October 7 the p_H was 5.0 and no pus was found. October 9, which was the ninth day of treatment, sterile cultures were obtained. No pus was present in the urine. The patient had taken only 8 ounces (235 cc.) of the medication, but, because of her excellent condition, treatment was discontinued. She returned for repeated examinations and on October 21 the urine was still free from pus, the p_H was 7.0 and she stated that she felt better than she had in a long time.

Case 16.—This is the second of the cases examined on the same day. It was stated that the pathologic condition was similar except that this patient was an older woman, aged 76, who had been ill for months. It was said that she was known to have diabetes, which makes it interesting because diabetic patients are considered to have less infection, owing to the ketone bodies in the urine. However her blood sugar was only 148 mg. and she had a one plus sugar in the urine. The pyelograms in this case show that there is even a more marked ptosis and hydronephrosis than there was in the preceding case. At the time of cystoscopy a cell count of from 8 to 10 per low power field was found in the left kidney urine and 200 or more in the right kidney specimen. Treatment was started October 1, and within seventy-two hours, without any other acidifying measures except the 40 per cent elixir of ammonium mandelate, the p_H of the urine dropped from above 7.0 to 5.0 and there was only a slight haziness to the urine.

Here the case became more interesting because on the third day after treatment was started the laboratory reported on the cultures made prior to treatment. The report was Bacillus proteus. Chute's[7] warning was recalled concerning the possibility of formation of urinary calculi when attempting to acidify a proteus infection because of the urea splitting properties of this bacillus, which produces ammonia. The urine thus made more alkaline would be predisposing to the formation of calcareous deposits. However as the p_H was 5.0 on the third day of treatment and the urine contained less pus, it was felt that we were justified in continuing the administration of ammonium mandelate. Seven days later the urine showed only 1 or 2 pus cells per high power field and the patient was feeling better in general, and though she had been bedfast for several weeks she was sitting up in a chair. The pain which she originally complained of in the right lumbar region had disappeared. October 13 an intravenous urogram was made. The blood chemistry showed a decrease in the sugar from 148 mg. to 120 mg. The nonprotein nitrogen decreased from 47 mg. to 35 mg. The intravenous urogram showed normal functioning of both kidneys with the same degree of dilatation and ptosis as previously seen. The urine culture is sterile and no pus is present in the specimen. She was taken off all therapy and given an unrestricted diet. She left the hospital October 20 with an increase in weight of 10 pounds (4.5 Kg.).

SUMMARY

The results obtained with the use of ammonium mandelate in treating sixteen cases of various types of urinary infection, regardless of the existing pathologic condition, may be thus summarized:

1. Seven cases of Bacillus coli infection resulted in six apparent cures and one partial cure with complications of hematuria in one case. There were no failures.

2. Three cases of staphylococcus infection resulted in three failures. One complicated with hematuria was followed by acute retention in a prostatic case with previous cerebral involvement.

3. One case of Streptococcus viridans infection was slightly improved.

4. One case of mixed infection of diplococcus and Streptococcus viridans resulted in apparent cure but there was a recurrence.

5. One case of diplobacillus infection resulted in apparent cure.

6. One case of mixed infection of staphylococci and diplobacilli and possibly tubercle bacilli resulted in failure with aggravation of all symptoms.

7. There was one mixed infection with gonorrhea in which treatment was not tolerated.

8. One case of Bacillus proteus infection resulted in apparent cure.

7. Chute, Richard: Urologist's Correspondence Club Letters, 3, March 23, 1936.

COMMENT

Rosenheim, in his study of mandelic acid treatment, concludes: "Mandelic acid appears to be effective in cases of urinary infection unassociated with urinary obstruction." It would seem that the explanation of apparent cure resulting in three cases, here reported, of marked obstruction is the fact that the drug is held longer in situ, thus giving its bacteriostatic powers longer time in which to function. The same reasoning seems logical in the cases of diverticula of the bladder in which such good results were obtained.

Because of the short period of time in which these cases have been observed, the good results have been designated as apparent cures only. Experience has shown recurrence in some cases.

Because of the increasing distribution of this drug for general use, without warning of possible complications, attention should be called to the complications encountered in this series of cases.

NOTE.—Since the presentation of this paper, personal communications from three other urologists, using ammonium mandelate from different pharmaceutical houses, have reported four cases of hematuria during its use.

1612 Edison Building.

AIR-BORNE INFECTION

SANITARY CONTROL

WILLIAM FIRTH WELLS, B.S.
AND
MILDRED WEEKS WELLS, M.D.
CAMBRIDGE, MASS.

In view of the proved possibility of infectious matter being carried by air, reasonable efforts to free air supplies from living micro-organisms are justified in the light of general sanitary principles. The great reduction of intestinal disease through water purification since the turn of the century might prompt us to hope that some of the diseases transmitted through discharges from the respiratory tract may be checked by methods of controlling air supplies. A study of the effect of ventilating factors on the dispersion and viability of micro-organisms suspended in air[20] has already disclosed the efficacy of certain destructive agencies.

Experiments on the disappearance of B. coli in the recirculated air of an air-conditioned room were conducted as a preliminary to the investigation of textile mill humidification referred to previously.[12] B. coli seemed to disappear much more rapidly from air when the spray humidifier was operating than when the air was recirculated without the use of the spray. Further tests showed that the reduction in the number of bacteria did not take place in the spray chamber but after the air had returned to the room, indicating that humidity might increase the death rate of B. coli in the air. Increasing relative humidity from 45 to 90 per cent more than doubled the disappearance of B. coli from air.

By means of the technic developed in this study, experiments on other physical and chemical factors were undertaken with the technical assistance of R. F. Wagner. Ozone in tolerable concentrations was found to give effects of a similar order of magnitude; i. e., olfactory concentrations four times the threshold value raised the death rate threefold. Commercial germicidal sprays also gave somewhat similar results. Negative and positive ions produced no observable differences in disappearance rate. The bactericidal action of a quartz mercury vapor lamp, however, was of a higher order of magnitude.[21]

The bactericidal effects of ultraviolet radiation on micro-organisms suspended in air proved to be of a higher order of magnitude than humidity, ozone or commercial germicides.

Effect of Ultraviolet Radiation.—Physical Factors:[22] These results precipitated an intensive investigation of the physical and biologic factors governing the effect of ultraviolet radiation on micro-organisms suspended in air.

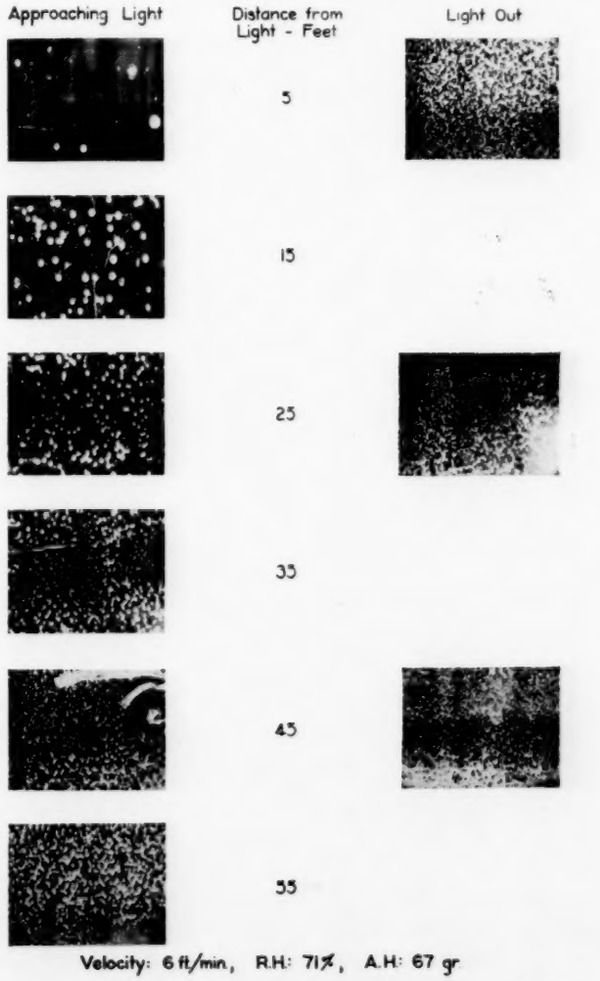

Fig. 2.—Bactericidal action of ultraviolet radiation on B. coli in air at different distances.

The interrelationship of space and time involved in the application of light to the sterilization of large volumes of air present mathematical problems hitherto unfamiliar either to sanitary science or to the science of illumination. In chemical disinfection, a relatively uniform concentration of active reagent is assumed for a disinfecting interval. In thermal sterilization or pas-

Second part of a paper read before the Harvard University Tercentenary (1636-1936) Symposium on "The Environment and Its Effect upon Man" at the Harvard School of Public Health, Aug. 24, 1936. The first part was published in THE JOURNAL, November 21, p. 1698.

20. A grant from the Milton Fund for studies on the defects of ventilating factors on dispersion and viability of micro-organisms suspended in air was made by Harvard University.

21. Wells, W. F., and Fair, G. M.: Viability of B. Coli Exposed to Ultraviolet Radiation in Air, Science **82**: 280 (Sept. 20) 1935.

22. Wells, W. F.: Some Basic Physical Factors Governing the Bactericidal Action of Ultraviolet Radiation on Micro-Organisms Suspended in Air. J. Bact., to be published.

teurization, each organism is subjected to a fairly uniform temperature for a specified interval of time. Where light has been used in the sterilization of liquids, a relatively thin film of exposure is necessary for effective action, so that each organism may be considered to be exposed to a relatively uniform degree of intensity of light for an adequate time interval. In attempting to

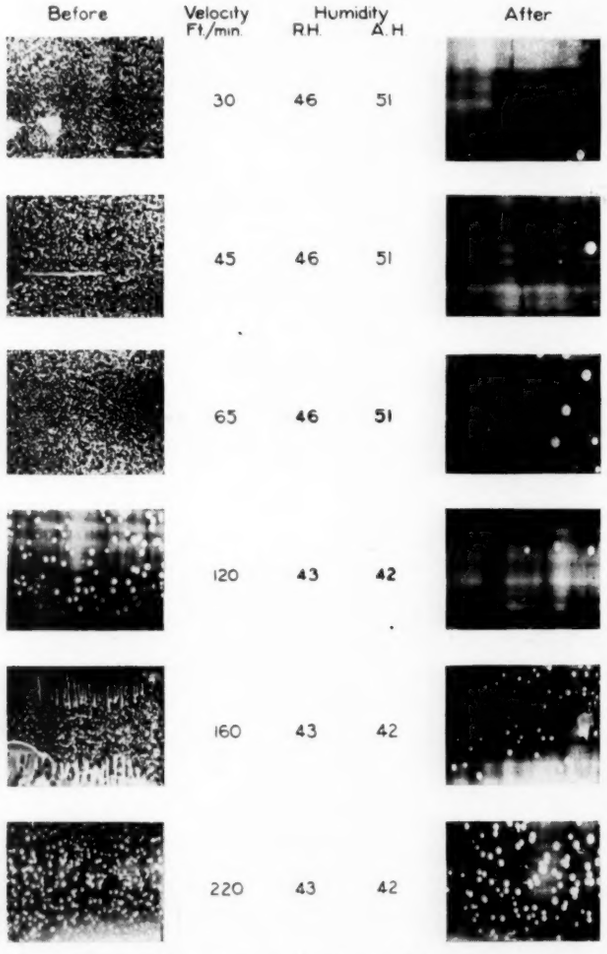

Fig. 3.—Bactericidal action of ultraviolet radiation on B. coli in air at different velocities. Passing light.

sterilize by ultraviolet rays the large volumes of air involved in practical ventilation, it becomes difficult if not impossible to maintain uniform light intensity throughout the ventilated space, or to maintain a constancy of exposure in so mobile a medium.

The first step in the solution of the time-space interrelationship was to develop means for determining the rate at which some test organism is killed at known distances from a given light. This cannot be done simply by exposing a quartz flask of air at some given distance from the light, because of the large volumes of air involved and the high cost of quartz. It was, however, possible to devise a dynamic method for exposing flowing air at predetermined distances from a given light for periods determined by the velocity of flow.

The number of organisms killed in moving from point to point toward a light can be determined. The integrated products of the times of exposure multiplied by the distances from the light then bears a simple relationship to the distances of the two sampling points from the light, by means of which the killing power constant of that light can be readily computed.

Preparatory to a more thorough analysis, and also to experimental application of light, studies were undertaken in the tunnel system of the Harvard School of Business Administration. A quartz mercury vapor lamp was placed in the center of this tunnel, which was 100 feet long, 8 feet wide and 7 feet high. Air inoculated with B. coli could be drawn down this tunnel at regulated velocities and the bacterial concentrations at different points determined by simultaneous sampling with three air centrifuges.

The bacterial reductions at flows above 20 feet per minute were too low for accurate determinations in approaching to within 5 feet from the light. Measurable reductions in bacteria were obtained with low air flows, but these low flows could not be accurately measured. At 6 feet per minute, bactericidal reductions could be determined and the flow measured with a reasonable degree of accuracy. The results of such a test are illustrated in figure 2. Marked reductions are apparent up to within 5 feet from the light, and noticeable effects as far as 55 feet from the light. Precise results could not be obtained by this method in the tunnel arrangement, though a more precise laboratory arrangement utilizing closer approach was later developed by Benjamin Whisler [23] in a study for a doctor's thesis.

Obviously the zone of greatest bacterial reduction lies within the sections 5 feet before and beyond the light.

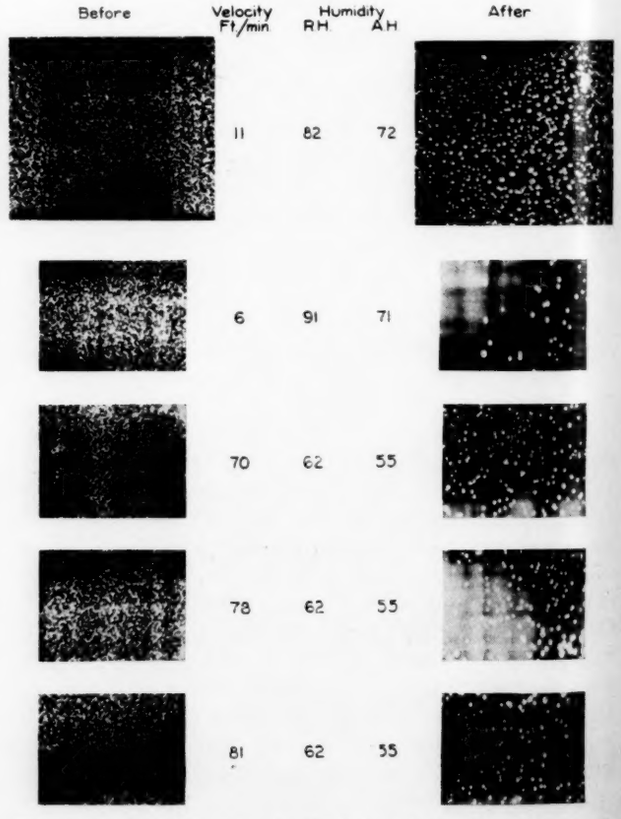

Fig. 4.—Bactericidal action of ultraviolet radiation on B. coli in air at different humidities. Passing light.

By sampling simultaneously at points upstream and downstream from the light, marked reduction in this tunnel was observed at velocities up to 222 feet per minute. The bactericidal effects in passing the light at six widely differing velocities under otherwise comparable conditions are illustrated in figure 3. More

23. Whisler, Benjamin: Unpublished thesis, Harvard University, 1936.

than half the bacteria were killed at velocities of 222 feet per minute, and yet some survived passage at a velocity of 30 feet per minute, which represents more than seven times the exposure.

Assuming the bacterial death rate to be proportional to the light intensity as given by the inverse square law for each point in space, it is possible to set up and integrate equations that can be tested by these experimental conditions.[24]

The values of $KI_0 \equiv K_0$, as given by these equations, with B. coli as the test organism, were found over the wide range of time-space variations, indicated by these tunnel experiments, to be constant within the errors expected from so simple an arrangement. Whisler's intensive studies with more refined apparatus confirmed the substantial validity of the assumptions and the practical applicability of the formulation. The values thus obtained for the constant K_0 justify the initial assumption, which may now be modified and stated in the following form:

The total number of given organisms killed by a given light is proportional to the total quantity of light energy intercepted by the living organisms and approaches a maximum as the product of time and intensity for each approaches uniformity.[20]

Humidity: For constant atmospheric conditions the value of I_0 in these equations defines the killing power of a given source against organisms having a vulnerability defined by K. The results illustrated in figure 3 were thus obtained under relatively uniform humidity. Comparison with the results given in figure 4 reveals amazing differences in bactericidal effect with different humidities. The results obtained at flows of 65 feet per minute shown in figure 3 are strikingly similar to the results shown in figure 4 for flows of only 6 feet per minute. This tenfold difference in killing power is the result of a difference in relative humidity between 45 and 90 per cent.

The numerical values of $\log \frac{N_0}{N_1}$ obtained in the tunnel experiments are plotted on figure 5 against the reciprocal of the velocity in conformity with the equations. It is seen from this chart that the results fall into two classes, each class represented by a straight line as would occur if K were constant for the class. The angle between the lines indicates a wide difference between the value for K for each class and it is seen that this difference corresponds to a difference in relative humidity, the killing power at low humidities being approximately ten times those obtained at high humidities. Since the inverse square law has been found to hold with high humidities as well as low humidities, the reduction in killing power appears to be due to interference with the bactericidal reaction on the bacteria.

The results of the more intensive study by Whisler clearly corroborate the relation between the vulnerability of B. coli and relative humidity. The values of $K_0 \equiv KI_0$ drop precipitately between relative humidities of 55 per cent and 65 per cent, above and below which the change is gradual, the values approaching constancy.

Obviously, humidity becomes a basic factor governing the bactericidal effect of ultraviolet radiations on bacteria suspended in air, the killing power for low humidities being manyfold that observed at higher humidities.

Spectral Range: Gates [25] has thoroughly investigated the lethal action of different wavelengths of light on bacteria smeared on agar plates. His conclusion that waves longer than 300 millimicrons are relatively ineffective has been confirmed for air suspensions of bacteria by filtering out these shorter waves. His conclusion that the maximum effect lies in a zone midway between 200 and 300 millimicrons would conform to the values of KI_0 obtained by lamps emitting different spectral ranges. The most efficient source among several types tested proved to be a 48 inch quartz Geisler mercury tube [26] emitting 90 per cent of its radiation as a wavelength of 254 millimicrons. Only 12 inches of a double arc gave a value for KI_0 of 910, at a relative humidity of 42 per cent, when tested against B. coli. Since this lamp consumes about 35 watts, the KI_0 approximates 50 per watt. If this value is applied in the preceding equations, it is seen that less than one colon bacillus per thousand suspended in several thousand feet of air would remain after irradiation with this light.

Those ultraviolet ray sources which emit the largest proportion of radiant energy midway between 200 and 300 millimicrons are most efficient in destroying microorganisms suspended in air.

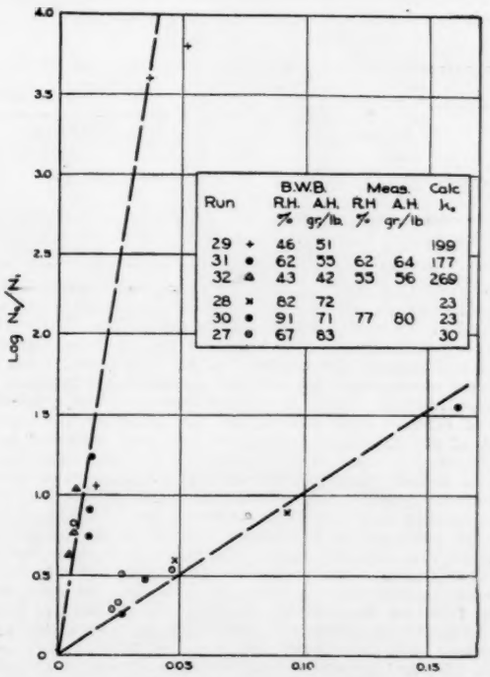

Fig. 5.—Effect of humidity on death of B. coli passing ultraviolet rays in tunnel.

24. The formulation for simple physical combinations are summarized: If N_0 = number of organisms before and N_1 = number of organisms after irradiation by light of lethal intensity I for time t, then $\log_e \frac{N_1}{N_0} = -KIt$; and at r distance from a source I_0, $= \frac{-KI_0t}{r^2}$; and in a sphere of R radius (source at center), maximum $= \frac{-3KI_0t}{R^2}$ for infinite mixing of air, and minimum $= \frac{-1.2KI_0t}{R^2}$ for zero mixing of air; and approaching a source at velocity v from $+\infty$ to r distance from source, $= \frac{-KI_0}{v\,r}$; and passing the source (from $+\infty$ to $-\infty$) on a straight line r distance from source, $= \frac{-\pi KI_0}{v\,r}$, and for a cylinder of R radius with source in axis (from $+\infty$ to $-\infty$). maximum $= \frac{-2\pi KI_0}{v\,R}$ for infinite turbulence, and minimum $= \frac{-1.24\pi KI_0}{v\,R}$ for stream line flow.

25. Gates, F. L.: A Study of the Bactericidal Action of Ultraviolet Light, J. Gen. Physiol. **13**: 231 (Nov.) 1929.

26. Kindly lent by the Hanovia Chemical Manufacturing Company.

Biologic Factors.—The bactericidal ranges of commercial ultraviolet lamps seemed to warrant experiments looking toward their practical application in sanitary air control. A therapeutic lamp was therefore set up in a clinic of the Children's Hospital, where the atmosphere had been found to build up a relatively high bacterial concentration during hours of active service. Preliminary tests, however, did not give the expected results. The lamp was found by test to be adequate and also proved in the clinic room to be effective against B. coli. If the presence of more resistant organisms was the explanation of these disappointing results, an important question was raised, since there is no hygienic significance in the elimination of B. coli from air. This study was therefore temporarily put aside until further information regarding the relative vulnerability of significant organisms to ultraviolet radiation could be ascertained. The equipment previously developed for determining the viability of droplet nuclei infection was therefore adapted to the study of the biologic factors bearing on the germicidal effect of ultraviolet radiation. Samples of air were withdrawn from the tank through siamized tubes to two Wells air centrifuges. One branch led directly to a centrifuge; the other branch included a small chamber enclosing a quartz Geisler mercury tube, by means of which the air passing to the second centrifuge could be irradiated with ultraviolet light. Organisms in the tubes taken at the Children's Hospital both before and after irradiation of the air were observed to be predominantly sarcinae and staphylococci, owing probably to the nature of the activities of that particular clinic. These organisms are characteristic of the skin and were raised into the air by the dressing and undressing of the patients, together with the treatments given, which consisted largely of massage, manipulative exercises, and so on. These organisms typically grow in clusters and are thrown into the air in masses, which may be a natural provision for the survival of organisms adapted to grow on surfaces, be rubbed off, and spread through the air to other surfaces. The relative coarseness of the suspended particles, as compared to droplet nuclei, was indicated by the ratio of bacterial counts on centrifuge tubes and on Petri plates, which was intermediate between the ratios found in the humidified weaving rooms and the dusty carding rooms of cotton mills.

TABLE 2.—*Relative Vulnerability to Ultraviolet Radiation of Individual Cells of Various Cocci Suspended in Air (B. coli 1.00)*

Organism	Number of Runs	Vulnerability	
		Constant	*K*
B. coli	20	1.00	
Streptococcus viridans	5	1.05	±.07
Staphylococcus albus	5	1.18	±.07
Staphylococcus aureus	7	1.21	±.20
Sarcina lutea*	3	0.85	±.02

* The chance that all eight cells of a packet will be killed is the eighth power of the chance that an individual cell in a packet will be killed. If one half of the cells in a packet lie in the shadow of the other half, and if the packet turns in such a manner that each cell shares equally the light and shadow, the chance of a cell in a packet being killed is one-half the chance when the cells are so distributed in space that no cell eclipses another. From the determination of the vulnerability of packets of sarcinae (0.083 when 66 per cent survived), the vulnerability constant of the individual sarcina cell has been computed as 0.85, if B. coli is given a value of one. Since, in the determination, packets flowed in a smooth stream past the light source in less than two seconds, it is doubtful whether each cell shared equally in light and shadow. Since exposure to equal quantities of light is the condition of maximum killing, the vulnerability of sarcina cells would be greater than is indicated by this computed value. The fact that doubling the intensity of the light increased the proportion of packets killed by only 7 per cent would indicate that a constant proportion of cells were thus protected from the light, owing to a constant condition of flow, which was not affected by changes in light intensity. From the figures, it would appear that more than half of the packets survived because of protected cells, and the vulnerability constant of individual sarcina cells is greater than one. The importance of illuminating particles on various sides becomes apparent.

The organisms first subjected to test in the experimental tank were the staphylococci and sarcinae isolated from the tubes taken at the Children's Hospital. The staphylococci were considerably more resistant than B. coli, sarcinae considerably more resistant than staphylococci. Alpha streptococci, on the other hand, were comparable in their vulnerability to B. coli.

The fact that the less vulnerable organisms were those which normally grow in masses and are separated only with difficulty suggested that their apparent resistance to light, as compared with those which separate naturally into individual unit cells, was due to this grouping. Streptococci, which divide in parallel planes, forming chains which are readily broken up, were comparable in their vulnerability to B. coli; staphylococci, which divide irregularly in more than one plane, resulting in cohesive grapelike clusters, were more resistant; while sarcinae, which divide in three planes at right angles to one another, forming packets with a minimum of eight cells, were still more resistant. To determine whether the manner in which organisms naturally group themselves was a prime factor in their varying resistance, cultures were grown in a revolving flask with suitable culture medium barely covering a layer of glass beads. Grinding during growth in this tiny ball mill, followed by prolonged centrifugating, provided a technic whereby suspensions consisting largely, though never entirely, of individual unit cells of streptococci and staphylococci could be tested against ultraviolet rays. Sarcinae, on the other hand, could not be broken down further than to the packet of eight cells, which seemed to constitute the basic unit.

In table 2 is given the vulnerability constant *K* for four organisms grown in the revolver, with B. coli for comparison. The differences in vulnerability between unit cells of streptococci and staphylococci, produced by this technic, and the naturally single cells of B. coli are within the limits of experimental error. The vulnerability constant for sarcinae, however, differs markedly from those for the other organisms. Presumably each of the eight cells in a packet is sufficient for reproduction, and it would be necessary to kill all eight to prevent a colony developing from a suspended packet.

The mathematical formulation employed in the derivation of the constant *K* for single cells must obviously be modified before application to multicellular groups of organisms. Under the conditions of the test, thirteen times as much light was required to destroy all eight of the cells grouped in a sarcinae packet as was required to kill each colon bacillus dispersed individually. This would conform to the assumption that the vulnerability of individual cells is likewise similar to that of the other organisms given in the table. A progressive increase in the vulnerability constant *K* during the course of the tests was observed for those organisms which tend to form clusters, but not for B. coli, as would be expected if the number of cells in the clusters is being reduced by a natural death rate. The implied assumption that only one light unit is required to destroy one life unit, which underlies the mathematical formulation, thus appears to be satisfied.

Cell units of the organisms so far tested, therefore, have proved to be equally vulnerable to ultraviolet radiation.

The study of the biologic factors underlying the vulnerability constants is far from complete. Such factors as capsule formation, spores and pigment remain to be explored. Ultimately the vulnerability constants of pathogens will be independently determined. The fact shown in table 2, that Staphylococcus aureus and Staphylococcus albus do not, in spite of the difference in pigment, differ markedly, suggests that the latter factor is not of the prime importance that might be imagined. There has not been enough work to indicate that more resistant organisms are not common. There is, however, sufficient evidence to indicate that B. coli is not peculiar in its susceptibility.

In the practical application of ultraviolet radiation it becomes evident that a distinction must be made between clumps and individual organisms, between dust and droplet nuclei. Air purification methods that depend on filtration or sedimentation may be more effective against dust, and ultraviolet rays may be more effective against nuclei, the two being complementary and therefore effectively combined. Likewise, methods that are effective in testing for one type of suspended organism may be inappropriate for testing the efficiency of purification devices against the other type.

Virucidal Action of Light:[11] The persistent belief that air may transmit certain virus diseases made it important to determine whether bactericidal light would also destroy air suspensions of virus. Into the air of the tank were atomized the filtrates of lung emulsions of ferrets made ill with the Puerto Rico 8 strain of influenza virus. Simultaneous sampling under identical conditions of air as it came from the tank and after ultraviolet irradiation indicated a definite virucidal action of the rays. In two tests the ferrets that were inoculated with material recovered from unirradiated tank air suffered a typical attack of influenza, which was confirmed by virus neutralization tests. The ferrets that received material simultaneously recovered from the air of the tank under identical conditions, except for irradation of the air, failed to show any symptoms of influenza, and virus neutralization tests subsequently showed no development of immunity.

The infectivity for ferrets of air suspensions of the Puerto Rico 8 strain of influenza virus was destroyed by ultraviolet radiation.

APPLICATION OF SANITARY AIR CONTROL

The question of air-borne infection will not be definitely answered until common air supplies are rendered free from nasopharyngeal contamination, just as endemic water-borne intestinal disease became apparent only with change from polluted to pure water supplies.

A solid foundation for sanitary air analysis has been developed, by which the purity of air can be determined, air contamination interpreted, and the efficiency of air purification processes tested. The practical effectiveness of certain devices that can be applied to the bacterial purification of air has been demonstrated. Others[27] have reported beneficial results following control of the bacterial content of the air of operating rooms. The experimental application of sanitary air control in hospitals, schools and other gathering places is indicated.

27. Hart, D.: Sterilization of the Air in the Operating Room by Special Bactericidal Radiant Energy, J. Thoracic Surg. 6: 45-81 (Oct.) 1936.

Clinical Notes, Suggestions and New Instruments

ANTERIOR LENTICONUS

E. C. MOULTON, M.D., FORT SMITH, ARK.

Anterior lenticonus is such an extremely rare condition that this case is presented briefly for consideration. All literature to date reveals only ten undoubted cases. Dr. Benjamin Rones reviewed these cases before this section in 1934. The case here presented is offered as the eleventh true type of anterior lenticonus.

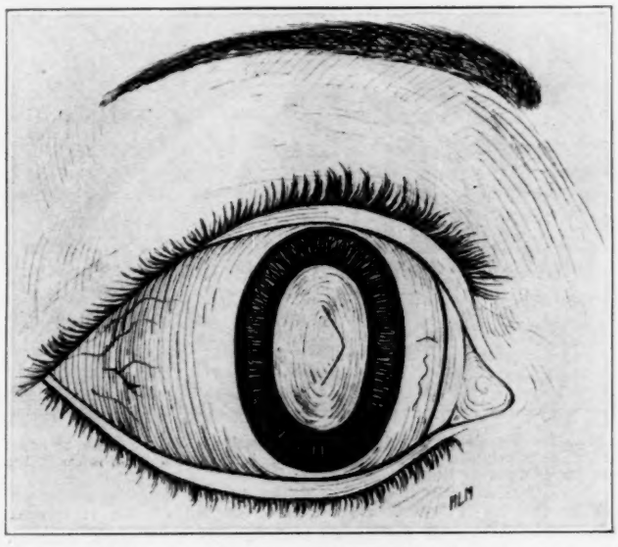

Fig. 1.—Right eye showing semidiagrammatically the extent and relative size of the cone.

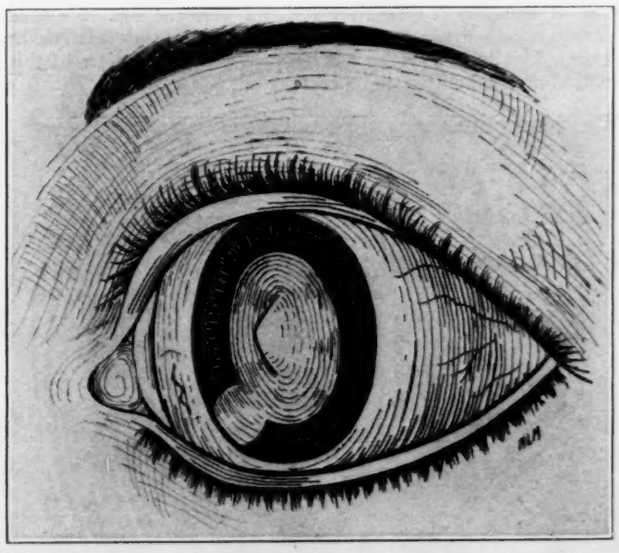

Fig. 2.—Same case as in figure 1 showing left eye, on which an optical iridectomy had been done.

REPORT OF CASE

S. W. H., a man, aged 33, came under observation in March 1927. Since the age of 17 he had been aware of poor vision, causing him to give up boxing and to be refused enlistment in the army. As a furnace builder in a glass factory he was considerably handicapped. Vision in a darkened room was:

Right 20/100 + 1.00 = 20/70
Left 20/70 + 1.00 = 20/50

When the refraction room was illuminated vision became reduced to 10/200 and did not admit of any improvement, this

Read before the Section on Ophthalmology at the Eighty-Seventh Annual Session of the American Medical Association, Kansas City, Mo., May 14, 1936.

change, of course, resulting from the alteration in the size of the pupil.

With the ophthalmoscope the usually described "oil drop" in the center of the pupil was noticed, and then by use of the loupe and focal light the anterior lenticonus could be detected. Under atropine the fundus could be seen nicely through the peripheral emmetropic lens substance and also a clear view was obtained through the apex of the cone with a minus 20.00

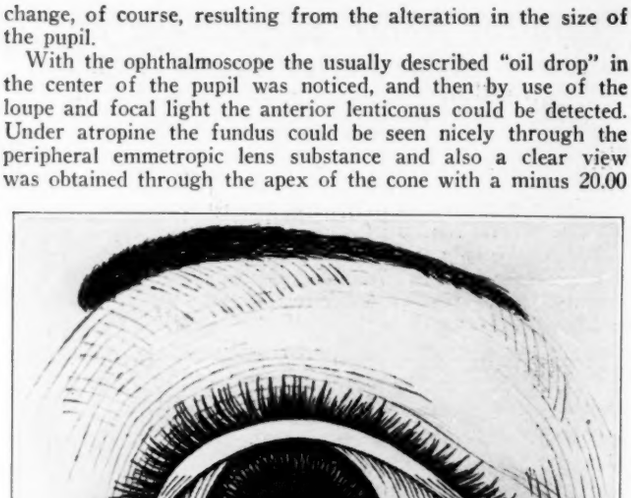

Fig. 3.—Slit lamp appearance with broad beam of light showing corneal parallelepiped and the beam of light traversing the lens with the cone on its anterior surface.

lens in the sight hole. With the exception of the lenticular defect in each eye all the media and fundus were quite normal. In a few days when the effect of the mydriatic had worn off and the pupil, in myosis, was again the size of the base of the cone, the patient reported and requested more atropine in his eyes. Reluctantly it was given him for personal use. He used it continuously against my advice, alternating eyes a week at a time. Finally in 1934 he was persuaded of the danger of this practice and submitted to operation.

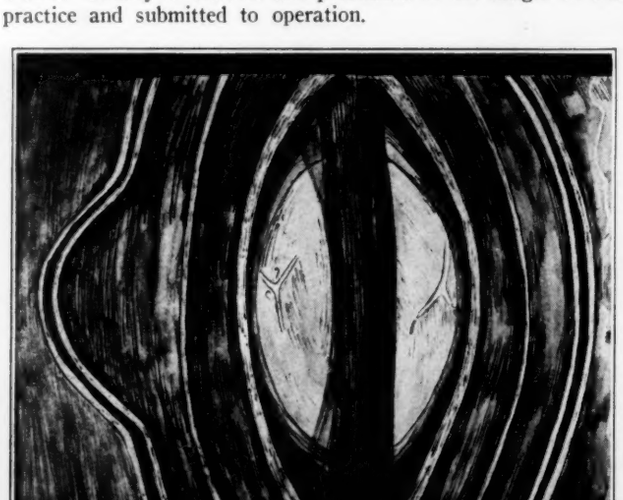

Fig. 4.—Optical section with very narrow light beam and full illumination. Only the anterior band of the lens and the anterior band of disjunction are involved, all the other zones of discontinuity being quite normal.

An iridectomy was done in the lower nasal quadrant of the left eye with resulting 20/50 vision and discontinuance of atropine. At no time have glasses been of comfort.

The microscopic examination of the lens with the slit lamp in January 1936 was most striking. With a broad beam of light the cone was clearly seen but it was with the very narrow beam and full illumination that the details in optical section are so instructive. The results are quite parallel to the reports of Kienecker [1] and Feigenbaum,[2] which are the only other two cases observed with the slit lamp. In this case only two zones of discontinuity are involved, namely the anterior band of the lens and the anterior band of disjunction. There are no accessory bands. These two bands bend forward over the clear underlying contents of the conus without alteration in their parallelism or change in thickness of either zone. The zones defining the adult nucleus and the fetal nucleus are quite normal, as are all the posterior bands. On the apex of each cone and situated just beneath the intact anterior capsule are a few very minute and delicate brown granular opacities.

Thus the three cases examined to date with the slit lamp must be of the acquired form of anterior lenticonus, and in this one, as in the other two, it is a question rather of lentiglobus than of lenticonus.

205 Merchants National Bank Building.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING ARTICLE. HOWARD A. CARTER, Secretary.

INTERFERENCE WITH RADIO COMMUNICATION BY THERAPEUTIC EQUIPMENT

H. B. WILLIAMS, M.D., Sc.D.
NEW YORK

There is hardly a home now which is without a radio-receiving set and hardly an individual who does not understand the meaning of the word "static" as used in connection with radio reception. While relatively little can be done at present to prevent disturbance by electrical storms, a great deal of disturbance for which Mother Nature has been blamed has originated in the activities of man. Some of this man-made "static" is unnecessary and most of it can be prevented for a price. Fortunately, in many cases, this price is not prohibitively high.

While the radio in the average home is largely a matter of entertainment and can be dispensed with when necessary, there are other uses, such as communication between ships and shore, aircraft and ground, and the transmission of directional signals, interference with which may easily result in loss of life.

Many of the members of the medical profession will learn with surprise that we have been, unwittingly, responsible for broadcasting a great deal of disturbance of a particularly annoying type. The most prominent offenders in our armamentarium are the various medical and surgical diathermy machines, particularly the new short wave diathermy and artificial fever devices.

Last winter important activities of the Naval Research Laboratory at Washington, D. C., were subjected to interference so serious as to stop the work completely. Eventually, after great trouble and expense, the disturbance was traced to therapeutic equipment. The first disturbing instrument located was a diathermy unit located in a hospital at Cambridge, Mass.

It is common knowledge that broadcasting stations make use of a large aerial structure to facilitate radiation of energy. Without such a structure the disturbance, unless exceptionally intense, is unlikely to be felt at great distances. The apparatus at Cambridge was found to have been so connected to the power supply line that the latter functioned as an antenna

1. Kienecker, R.: Klin. Monatsbl. f. Augenh. **82**: 55 (Jan. 25) 1929.
2. Feigenbaum, A.: Folia ophth. orient. **1**: 103 (Nov.) 1932.

and enabled this small apparatus to broadcast a "sky wave" of considerable intensity. The insertion of a suitable electric filter between the apparatus and the power line was all that was necessary to stop most of the trouble. It is of interest to know that this equipment was supplied and installed by an electrical manufacturer who also supplies vast quantities of radio equipment and is vitally interested in avoidance of interference. In view of this I think that the medical profession may be forgiven for the trouble that has occurred in the past; but now that the facts are known every effort should be made to minimize the evil.

It is expected that the Council on Physical Therapy of the American Medical Association will presently alter its requirements for acceptance of electrical equipment such as is known to have caused interference. Manufacturers will be asked to submit evidence that the construction and installation specifications are such as to prevent interference.

Even though an apparatus may not broadcast an intense sky wave, it will, unless properly filtered, cause disturbance of every radio receiving set which derives power from the same line, thus becoming a nuisance even if it escapes being a menace.

It is confidently expected that users of existing equipment purchased from reliable manufacturers will be able to secure from the manufacturers such additional equipment and engineering advice as will make it possible to prevent interference. Any one who has difficulty in obtaining the desired information or equipment is invited to communicate with the Secretary of the Council on Physical Therapy of the American Medical Association.

It is imperative that the medical profession and the manufacturers of electrical equipment for the profession take prompt steps to abate this nuisance, as otherwise it is certain that relief through legislation will be requested. This is liable to bring undesirable restrictions and will probably be entirely unnecessary if suitable action is initiated by the profession itself.

Council on Foods

ACCEPTED FOODS

THE FOLLOWING PRODUCTS HAVE BEEN ACCEPTED BY THE COUNCIL ON FOODS OF THE AMERICAN MEDICAL ASSOCIATION FOLLOWING ANY NECESSARY CORRECTIONS OF THE LABELS AND ADVERTISING TO CONFORM TO THE RULES AND REGULATIONS. THESE PRODUCTS ARE APPROVED FOR ADVERTISING IN THE PUBLICATIONS OF THE AMERICAN MEDICAL ASSOCIATION AND FOR GENERAL PROMULGATION TO THE PUBLIC. THEY WILL BE INCLUDED IN THE BOOK OF ACCEPTED FOODS TO BE PUBLISHED BY THE AMERICAN MEDICAL ASSOCIATION.

FRANKLIN C. BING, Secretary.

SEXTON BRAND BARTLETT PEARS, JUICE PACKED

Manufacturer.—John Sexton & Company, Chicago.

Description.—Canned pears packed in juice.

Manufacture.—Bartlett pears harvested green are stored to reach proper degree of ripeness, graded, mechanically peeled, cut, stemmed, inspected, brined, rinsed and placed in cans. The cans are automatically filled with fruit juice, exhausted, sealed and processed at 100 C.

Analysis (submitted by manufacturer).—(Analysis of entire contents including liquid): moisture 87.0%, total solids 13.0%, ash 0.3%, fat (ether extract) 0.1%, protein (N × 6.25) 0.2%, crude fiber 0.5%, carbohydrates other than crude fiber (by difference) 11.9%.

Calories.—0.49 per gram; 14 per ounce.

Claims of Manufacturer.—For diets in which sweetened fruit is proscribed.

(a) OUR PRIDE BRAND CRYSTAL WHITE SYRUP
(b) OUR PRIDE BRAND GOLDEN TABLE SYRUP

Distributor.—Meyer Schmid Grocer Company, St. Louis.

Packer.—Union Starch and Refining Company, Granite City, Ill.

Description.—(a) A table syrup; corn syrup sweetened with sucrose; flavored with vanilla extract—the same as Pennant Crystal White Syrup (THE JOURNAL, Jan. 30, 1932, p. 403). (b) A table syrup; corn syrup flavored with refiners' syrup—the same as Pennant Golden Table Syrup (THE JOURNAL, Jan. 30, 1932, p. 403).

Claims of Manufacturer.—For table use and as a carbohydrate supplement for milk modification in infant feeding.

SEXTON BRAND APPLE SAUCE, JUICE PACKED

Manufacturer.—John Sexton & Company, Chicago.

Description.—Canned apple sauce prepared from peeled and cored apples.

Manufacture.—Blended varieties of western New York apples, tree ripened, are hand picked, spray washed, mechanically peeled and cored, inspected, washed in salt water, and cooked to the proper degree. Seeds and fibrous parts are removed by pulping machine and the apple sauce is hermetically sealed and processed.

Analyses (submitted by manufacturer).—(Analysis of entire contents including liquid): moisture 87.7%, total solids 12.3%, ash 0.24%, fat (ether extract) 0.2%, protein (N × 6.25) 0.2%, crude fiber 0.46%, carbohydrates other than crude fiber (by difference) 10.2%.

Calories.—0.43 per gram; 12 per ounce.

Claims of Manufacturer.—For diets in which sweetened fruit is proscribed.

GOLDEN DRIP BRAND SYRUP
SILVER DRIP BRAND CRYSTAL WHITE SYRUP

Distributor.—Empire Distributing Co., St. Louis.

Manufacturer.—Union Starch & Refining Co., Granite City, Ill.

Description.—1. A table syrup; corn syrup flavored with refiners' syrup; the same as Pennant Golden Table Syrup (THE JOURNAL, Jan. 30, 1932, p. 403). 2. A table syrup; corn syrup sweetened with sucrose; flavored with vanilla extract; the same as Pennant Crystal White Syrup (THE JOURNAL, Jan. 30, 1932, p. 402).

APOLLO BRAND TOMATO JUICE

Distributor.—Halpen-Green Company, Philadelphia.

Packer.—Vincennes Packing Corporation, Vincennes, Ind.

Description.—Pasteurized tomato juice with added salt; retains in high degree the vitamin content of the raw juice. (The same as Alice of Old Vincennes Tomato Juice, THE JOURNAL, Feb. 20, 1932, p. 640.)

GROSSE POINTE BRAND FANCY CRUSHED HAWAIIAN PINEAPPLE

Distributor.—R. Schayowitz & Sons, Detroit.

Packer.—Hawaiian Pineapple Company, San Francisco.

Description.—Canned pineapple packed in concentrated pineapple juice with added sucrose. The same as Dole canned pineapple (THE JOURNAL, April 8, 1933, p. 1106).

HEART OF AMERICA BRAND TOMATO JUICE

Distributor.—Christopher Sales Company, Kansas City, Kan.

Packer.—Vincennes Packing Corporation, Vincennes, Ind.

Description.—Pasteurized tomato juice with added salt; retains in high degree the vitamin content of the raw juice; the same as Alice of Old Vincennes Tomato Juice (THE JOURNAL, Feb. 20, 1932, p. 640).

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, NOVEMBER 28, 1936

PHYSICIANS AND OLD AGE PENSION TAXES UNDER THE SOCIAL SECURITY ACT

Preliminary procedures are under way to make effective the old age benefit provisions of the Social Security Act. The regulations that have been promulgated by the Bureau of Internal Revenue looking toward the assembly of the mass of detailed data with respect to the employers and employees from whom the taxes are to be collected are of immediate interest to physicians.

Each person who on November 16 was the employer of one or more persons, subject to the exceptions noted, must have reported that fact prior to November 21 to the postmaster from whose post office the employer obtained his office or business mail. He must also have made application on form SS-4 for the assignment of a number—an "identification number" to be used for identification purposes in connection with the collection of taxes under the act. Physicians who were employers on the date named were required to comply with this requirement. If they failed to do so they should now communicate with their local postmasters for instructions as to how to proceed to make the delayed application. A physician who became an employer after November 16 must also apply for an identification number within a period of thirty days after the relationship of employer and employee is established. This application, the regulations provide, must be made to the field office of the Social Security Board in the area in which the office of the physician is situated or, in the absence of such field office, to the Social Security Board at Washington, D. C.

Persons who were employees on November 24 are likewise required to obtain numbers, called "account numbers," by filing application on form SS-5, on or before December 5, with the local postmaster. Persons becoming employees after November 24 must also file application for numbers thirty days after the employment begins. While physicians generally are considered, under the regulations, as independent contractors and consequently not subject to the taxes imposed on employees, if physicians are employed on a full time or part time salary basis they are apparently to be considered as employees. Such physicians must file application for "account numbers" on form SS-5. As employees they are subject to the tax on employees, and their employers must pay the employer's tax with respect to them.

Certain employments do not come within the old age benefit provisions of the Social Security Act. Among the exceptions are agricultural labor, domestic service in a private home, casual labor not in the course of the employer's trade or business, service performed by an individual who has attained the age of 65, service performed in the employ of the United States or of any state or subdivision or instrumentality of either, and service performed in the employ of a corporation, community chest, fund or foundation organized and operated exclusively for religious, charitable, scientific, literary or educational purposes, or for the prevention of cruelty to children or animals, no part of the net earnings of which inures to the benefit of any private shareholder or individual. Physicians who employ only persons embraced within these excepted employments or who are themselves engaged in such excepted services are not required to make application for identification or account numbers.

Employers' and employees' taxes will be collected by means of monthly returns to be filed by employers, who not only must pay to the local collector of internal revenue the tax imposed on employers but also must deduct from the wages of their employees the employee's tax and transmit that also to the collector. The first returns will be due not later than March 1, 1937, covering wages paid for services rendered during the month of January. The regulations that have been promulgated cover in detail the records that must be kept by employers, the method of executing returns, the information they must contain and other matters relating to the tax. Physicians should promptly familiarize themselves with all the requirements, so that as much confusion as possible may be avoided. THE JOURNAL will from time to time offer suggestions to aid physicians in meeting the requirements of the act.

MYASTHENIA GRAVIS

Myasthenia gravis was first described by Willis [1] in the seventeenth century. For years it was considered a neurologic disorder even though investigators did not find any constant or characteristic lesion of the central or peripheral nervous system. Jolly [2] in 1895 suggested that the disease might be primarily one of the muscles. Later the muscular localization of this disorder was more firmly established by Buzzard's [3] demonstration that lymphocytic infiltration was more or less consis-

1. Willis, quoted by Guthrie, L. G.: "Myasthenia Gravis" in the Seventeenth Century, Lancet **1**: 330 (Jan. 31) 1903.
2. Jolly, F.: I. Ueber Myasthenia gravis pseudoparalytica, Berl. Klin. Wchnschr. **32**: 1 (Jan. 7) 1895.
3. Buzzard, E. F.: Myasthenia Gravis, Tr. Path. Soc. London **56**: 355, 1905.

tently a pathologic characteristic of the muscle fibers of patients who had the disease. These fundamental observations impelled investigators in the field definitely to shift their interest from the nervous to the muscular system. Meanwhile hyperplasia of the thymus, in association with myasthenia gravis, was noted by Oppenheim[4] in 1899. Subsequently hyperplasia of the thymus was found in nearly half of the cases in which necropsy was performed. This was sufficient to cause many investigators to consider such enlargements as of etiologic significance. Nearly every other ductless gland also has been incriminated, but there is a distinct lack of any substantial evidence of their participation in the syndrome.

Finally it was recognized that in this disease some phase of muscle metabolism was disturbed. The finding of creatine in the urine of a few patients who had myasthenia gravis, coupled with the known importance of phosphocreatine in muscle metabolism, stimulated interest in the possibility that the disease was primarily one of intermediary muscle metabolism. Evidence of a specific disturbance of metabolism, however, has not been obtained by the methods of investigation at present available, as has been shown by the comprehensive chemical studies by Boothby and his co-workers.[5] Creatinuria was observed in only seven of their thirty cases; however, after the daily administration of aminoacetic acid was started there developed a definite increase in the amount of creatine excreted by those who had a previous creatinuria; and a creatinuria developed to a greater or less degree in those who did not previously excrete creatine. A similar increase in creatinuria also occurs in most normal persons after the ingestion of aminoacetic acid. Some investigators have conjectured that the site of the process responsible for the fatigability characteristic of the disease is at the myoneural junction. Most, however, are still satisfied that the disturbance of function is within the muscle fiber; they leave the mechanism of the disturbance and its exact localization within the muscle fiber in the realm of speculation.

Associated closely with the advancing knowledge of myasthenia gravis has been the study of the chemical mediation of nerve impulses. Recent research[6] indicates that acetylcholine is liberated on stimulation of motor nerves to voluntary, striated muscle. It is further recognized that physostigmine and prostigmin[7] probably prevent destruction of acetylcholine by inhibition of the normal blood choline esterase. Concentration of this esterase has been reported by Stedman[8] to be low in one case of myasthenia gravis. Potassium chloride,[9] when injected into the arteries of cats, will cause release of acetylcholine from tissues of which the innervation is cholinergic. These interesting observations merit consideration in view of their obvious importance in interpretation of the pathogenesis of the disease. However, to attempt at present a deduction from the information available might result in many fallacious concepts. This most recent work obviously does not tell the whole story. Boothby[10] has aptly stated that investigators are still ignorant of the cause of the disturbance in the contracting mechanism, which is an important feature of myasthenia gravis.

Many investigators have noted the relationship between myasthenia gravis and infection, especially infection of the upper part of the respiratory tract, and some of them have suggested, without direct evidence, that a toxin, probably of microbic origin, is the agent responsible for some type of chemical upset causing the characteristic fatigability. In a recent study Butt[11] has demonstrated gram-positive diplococci within or between the muscle fibers in some of the sections of muscle in seven cases of myasthenia gravis. Norris[12] also has demonstrated micro-organisms in the muscles of a patient who had this disease; but since he found them also in the muscles of a patient who had Addison's disease and in those of normal controls he was not inclined to consider their presence as significant. Rosenow and Heilman[13] have successfully taken cultures and identified streptococci from patients who had the disease and have produced the clinical and pathologic picture in animals by inoculating them with these organisms. It remains for future investigations to determine whether these organisms are the agents responsible for this syndrome.

Some of the most important recent contributions in the study of myasthenia gravis have been in treatment. The beneficial effect of ephedrine was demonstrated by Edgeworth[14] in 1930, and the value of aminoacetic acid was pointed out simultaneously by Remen[15] and by Boothby[16] in 1932 following the report of Thomas,

4. Oppenheim, quoted by Skinner, E. F.: A Case of Myasthenia Gravis, J. Neurol. & Psychiat. **4:** 344, 1924.

5. Boothby, W. M.; Adams, Mildred, and Power, M. H.: Myasthenia Gravis: Second Report on the Effect of Treatment with Glycine, Proc. Staff Meet., Mayo Clin. **7:** 737 (Dec. 28) 1932. Adams, Mildred; Power, M. H., and Boothby, W. M.: The Influence of Glycine on the Excretion of Creatine and Creatinine, Am. J. Physiol. **111:** 596 (April) 1935; Chemical Studies in Myasthenia Gravis, Ann. Int. Med. **9:** 823 (Jan.) 1936.

6. Dale, H. H.; Feldberg, W., and Vogt, M.: Release of Acetylcholine at Voluntary Motor Nerve Endings, J. Physiol. **86:** 353 (May 4) 1936. Lindsley, D. B.: Myographic and Electromyographic Studies of Myasthenia Gravis, Brain **58:** 470 (Dec.) 1935.

7. Prostigmin is the dimethyl carbamic ester of hydroxyphenyltrimethyl ammonium methylsulfite.

8. Stedman, Edgar: The Choline Esterase Content of Blood in Myasthenia Gravis, J. Physiol. **84:** 56P, 1935.

9. Feldberg, W., and Guimaráis, J. A.: The Liberation of Acetylcholine by Potassium, J. Physiol. **86:** 306 (March 9) 1936.

10. Boothby, W. M.: Myasthenia Gravis: Seventh Report, Medical papers dedicated to Dr. Henry A. Christian, February 1936, p. 883.

11. Butt, H. R.: Myasthenia Gravis: A Study of Postmortem Observations, Including the Demonstration of Gram-Positive Bacteria (Streptococci) In and Between the Muscle Fibers, Arch. Path. **21:** 27 (Jan.) 1936.

12. Norris, E. H.: The Thymoma and Thymic Hyperplasia in Myasthenia Gravis with Observations on the General Pathology, Am. J. Cancer **27:** 421 (July) 1936.

13. Rosenow, E. C., and Heilman, F. R.: Serologic Studies with Streptococci Isolated in Cases of Myasthenia Gravis, Proc. Soc. Exper. Biol. & Med. **34:** 477 (May) 1936.

14. Edgeworth, Harriet: A Report of Progress on the Use of Ephedrine in a Case of Myasthenia Gravis, J. A. M. A. **94:** 1136 (April 12) 1930.

15. Remen, L.: Zur Pathogenese und Therapie der Myasthenia gravis pseudo-paralytica, Deutsche Ztschr. f. Nervenh. **128:** 66, 1932.

16. Boothby, W. M.: Myasthenia Gravis: A Preliminary Report on the Effect of Treatment with Glycine, Proc. Staff Meet., Mayo Clin. **7:** 557 (Sept. 28) 1932.

Milhorat and Techner [17] on the improvement in fatigability following the administration of aminoacetic acid to a patient who had progressive muscular dystrophy. Knowledge of the effects of these substances has almost completely changed the course of treatment and the prognosis. In addition, the fact that physostigmine,[18] prostigmin [19] and potassium chloride [20] exert favorable effects on patients who have myasthenia gravis have stimulated a great amount of interest in treatment of the disease.

Boothby [21] has emphasized the fact that the disease is of long duration and that no single therapeutic procedure or any one drug cures the disease. Therefore the patient must be educated to avoid so far as possible the dangerous complications of myasthenia gravis; also all available therapeutic procedures must be utilized to decrease the characteristic fatigability. Of the eighty-two patients treated by Boothby, fifty are now working either full time or part time and although such results, in such a large series, are unusually favorable, there is still urgent need for continuation of carefully conducted and controlled studies of this disease.

Current Comment

INFLUENZA IN THE UNITED STATES

During eleven of the seventeen years since the summer of 1919, recognizable outbreaks of influenza have occurred. Since one of the chief characteristics of an influenza epidemic is the suddenness of its outbreak and the rapidity with which it spreads over a large area, any unusual increase in the number of reported cases of influenza in one locality is usually viewed with alarm. Miss Gover [1] has recently studied the epidemic of the past winter in the West South Central section of the country and elsewhere with a view to determining whether any greater outbreak is foreshadowed by the existing situation. Throughout the period of the epidemic of 1936 California was reporting more than the average number of cases of influenza for preceding years, but the curve of mortality for the Pacific section was only slightly higher than normal. By May 2 the California cases had dropped to normal. During the five weeks from May 31 to July 4 California reported 2,177 cases of influenza as against an expectancy of 124, or an excess of 2,053 cases. A summer rise, such as this, is unusual, but there was no parallel rise in mortality, and since July 4 through September 19 California as well as the Pacific area has been reporting only an average number of cases for that season of the year. The author concludes, therefore, that although an epidemic of influenza may occur this winter, the recent mortality from influenza does not indicate that such an epidemic is in progress in any section of the country at the present time.

17. Thomas, Karl; Milhorat, A. T., and Techner, Fritz: Untersuchungen über die Hurkunft des Kreatins: Ein Beitrag zur Behandlung progressiver Muskelatrophien mit Glykokoll (Vorläufig Mitteilung), Ztschr. f. physiol. Chem. **205**: 93, 1932.

18. Walker, M. B.: Treatment of Myasthenia Gravis with Physostigmine, Lancet **1**: 1200 (June 2) 1934.

19. Everts, W. H.: The Treatment of Myasthenia Gravis by the Oral Administration of Prostigmine, Bull. Neurol. Inst. New York **4**: 523 (Dec.) 1935. Laurent, L. P. E.: Clinical Observations on the Use of Prostigmine in the Treatment of Myasthenia Gravis, Brit. M. J. **1**: 463 (March 9) 1935. Minski, Louis, and Stokes, A. B. Treatment of Myasthenia Gravis, ibid. **1**: 1095 (May 30) 1936. Pritchard, E. A. B.: The Use of "Prostigmine" in the Treatment of Myasthenia Gravis, Lancet **1**: 432 (Feb. 23) 1935. Wade, H. J.: Treatment of Myasthenia Gravis, Brit. M. J. **1**: 1099 (May 30) 1936.

20. Laurent, L. P. E., and Walther, W. W.: Influence of Large Doses of Potassium Chloride on Myasthenia Gravis, Lancet **1**: 1434 (June 22) 1935.

21. Boothby, W. M.: Myasthenia Gravis: The Effect of Treatment with Glycine and Ephedrine; Third Report, Arch. Int. Med. **53**: 39 (Jan.) 1934; Eighth Report, Tr. A. Am. Phys., to be published.

1. Gover, Mary: Influenza Mortality in the United States, 1936, Pub. Health Rep. **51**: 1399 (Oct. 9) 1936.

THE ARMY MEDICAL LIBRARY—ONE-HUNDREDTH ANNIVERSARY

The one-hundredth anniversary of the Army Medical Library was celebrated in Washington November 16 with appropriate ceremony. High tribute was paid in a message by President Roosevelt. The librarian, Col. Harold W. Jones, reviewed its development and Surgeon General Reynolds introduced the centennial speaker, Sir Humphry Davy Rolleston, Bart., who had come from England especially for this occasion. In a scholarly address he reviewed the history of medical museums and libraries and the biographies of the great bibliographers—Billings, Fletcher and Garrison—who had been associated with the Army Medical Library in its growth. The occasion served incidentally to call attention to the pressing need for new quarters, the invaluable collection of books and documents being housed in a half-century old, non-fireproofed structure. THE JOURNAL again felicitates the Library on its marvelous record and expresses the wish that its hope for a new and suitable home may soon be realized.

IN HONOR OF DR. HUGH TALBOT PATRICK

The issue of the *Archives of Neurology and Psychiatry* for November 1936, which has just come from the press, is a special number dedicated to Dr. Hugh Talbot Patrick by his pupils. It contains in addition to notes of appreciation by Drs. Peter Bassoe, Chicago, Bernard Sachs, New York, and Professeur Georges Guillain, Paris, contributions on neurologic topics by these writers and many others who have from time to time been associated with Dr. Patrick in his work. To Dr. Hugh T. Patrick particularly must be assigned the credit for the initiation of the *Archives of Neurology and Psychiatry* as a publication in this special field. Dr. Sachs well states that this publication has done much to place American neurology and psychiatry on the highest scientific level. It has reflected constantly the progress of American medicine in this field. In listing the contributions of Dr. Patrick, special mention is given to his articles on arteriosclerosis of the nervous system, chronic progressive hemiplegia, the motor neuron in practical diagnosis, the proper care and treatment of the patient with epilepsy, syphilis of the nervous system, and the factor of fear in nervous diseases. More recently a number of excellent contributions have indicated his interest in biography and in the historical

aspects of neurology. The dedication of such volumes to men of leadership who have contributed as greatly as has Dr. Hugh T. Patrick toward medical advancement is a commendable gesture in a too careless and hastening age.

Medical Economics

THE NATURE OF PANEL PRACTICE IN ENGLAND

Some Evidence from the Pages of the British Medical Journal

A series of letters from physicians in the correspondence department of the *British Medical Journal* in recent months indicates that the physicians practicing under the panel system are by no means wholly satisfied with the character of service they are required to give. The letter that started the trouble was from F. S. Taylor-Thomas,[1] who wrote from Australia and says:

> My interpretation of the statement is that panel practice in action tends to produce the following:
>
> Patient (entering consulting room, and taking seat on chair) "I want somethin' for this wheezin' on my chest, Doctor. I've had it for a week now. Cough at night somthin' awful."
>
> Doctor: "Very well, take off your things and I'll examine your chest."
>
> Patient: "Oh, never mind that, Doctor! Just give me a bottle of cough mixture—some of that black stuff—and I'll be all right. I just called in as I was passin' up the street and thought I'd better get something before it gets worse."
>
> Doctor (glimpsing in the waiting room a crowd of other patients who just called in as they were "passin' up the street"): "Very well. Here you are." (Hands him prescription for mist. tussis, fishes out his panel card, enters date, diagnosis, treatment, etc., "shoos" him out to make way for another who wants something for his rheumatiz in the shoulder—and so the process is repeated.)
>
> Well, isn't that mechanization? Is that all an M.B., B.S. or M.R.C.P. has to do? Has he any chance, or is he allowed to do much, in the ordinary conditions of panel practice? What is the general practitioner in England today but a glorified first-aid man? Quack patients beget quack doctors. It is a question, from the general practitioner's point of view, of getting as many patients as he can on his list and getting the consultations over as fast as he can. Only by such means can a living be made. If the doctor comes across an illness which may interest him, had he the time and were he reasonably paid to treat it, he simply refers the patient to the nearest hospital; insurance committees do not encourage academic excursions by general practitioners. . . . if these people who are patients had only to pay 3d. to see the doctor it would cut down England's drug bill by half.

This letter very clearly started something. The next communication, by a writer under the name of "Juvenis," [2] and who is apparently a panel practitioner, adds this comment:

> I am convinced the majority of panel patients do not get full enough investigation. My surgery hours are cluttered up with people who certainly would not come so often or drink so much medicine if they had to pay even one penny a visit. I cannot do otherwise than rush them through. Those who are obviously ill, or who fail to regain good health after a reasonable lapse of time, are examined more carefully at home or out of surgery hours; but this method is only a makeshift, and I remember with dissatisfaction two carcinomata of the stomach recently diagnosed too late and a latent pulmonary tuberculosis labeled neurotic.

These criticisms brought Alfred Cox,[3] former secretary of the British Medical Association, to the defense with this statement:

> I have no doubt that "Juvenis" is sincere in his opinion about the panel system and as to the methods adopted in his practice. But I should be very sorry—and indeed I refuse—to believe that his experience is typical. I have had the good fortune to come in close contact with many busy insurance practitioners who have never had any doubt as to their ability to give their panel patients that which they contract to give—namely, a good general practitioner service.

Dr. Cox gives a statistical study of the services needed in an average panel list of 1,000 and concludes:

> I submit that in a well-organized practice every patient needing it could have the thorough examination that he or she ought to have. In times of epidemics, of course, all patients have to take what it is possible to give, but in many cases detailed examination can be deferred for a time.

In a later issue another doctor [4] says:

> I have been chairman of the Ross and Cromarty Insurance Committee for several years. I have also been chairman of the Ross and Cromarty Panel Committee for many years, and my index list is one of the largest in this area. I should thus know something of national health insurance practice, its good qualities and its bad qualities.

On the basis of this experience he gives as his opinion: "In the large majority of cases national health insurance practice is of a very high standard, and is not second to the standard of efficiency and rectitude attained by any other profession or business; otherwise, would it for one moment be tolerated by the public?" However, in the same issue Dr. Cox's statistical study is criticized with the following conclusion:

> Thus Dr. Cox's own figures suggest that a rush is probably a normal state in general practice for a considerable portion of the year. Most general practitioners are only too aware of this uncomfortable period when patients, panel and private, and their medical attendants suffer from the rush of work. Dr. Cox and the travelers in statistics from the Ministry of Health appear to be uninformed of this rush period, or rather the length of its duration. . . . Again, assuming Dr. Cox's figures to be correct, we find that an attendance on a panel patient is valued at rather less than two shillings. The remedy for this unsatisfactory state of affairs, as was pointed out a fortnight ago, is a revision of fees, both private and panel.

This conclusion as to payments to physicians is confirmed by the statement of another panel practitioner in the same issue who says:

> One wonders whether or not Dr. Cox is quite satisfied that the doctors receive an adequate remuneration for this "good general service," as it would appear to be more or less the consensus of opinion that the doctors themselves are not satisfied with their remuneration.

The controversy continues in the issue for October 17. One writer [5] comments:

> Many panel patients are irresponsible individuals unfit to enter into a contract with a doctor. These time wasters and the low capitation fee cause some dissatisfaction with the national health insurance service. Is the extent of this dissatisfaction known? Prosperous practitioners occupying prominent positions are unlikely to be dissatisfied, and tend to discourage admission of misgivings by their less fortunate professional brethren. Could not a confidential questionary be sent to every panel practitioner so that the truth may be discovered?

"Juvenis" returns to the discussion with a further examination of Dr. Cox's calculations and adds:

> A good examination in the surgery takes considerably longer than five minutes. Can any one examine a man for life insurance in five minutes? Moreover, in a practice like this, covering a scattered area of some thirty square miles, fifteen minutes per visit is too low an average of time consumption. Indeed, it is very difficult to find time and energy to read and think about my patients. And even when I do, economic considerations often restrict me to the palliative bottle of medicine. Indeed, I wonder if panel treatment is intended to be more than symptomatic. Of about one hundred formulae for misturae in the N. H. I. Formulary some fourteen are "cough mixtures"! How many dyspeptics can afford artificial teeth? How can one get a walking caliper for a fractured neck of the femur? How can one treat the host of psychopathic cases when neither the patient's approved society nor the regional medical officer seems to care a jot about treatment?

The editor then states that it is now necessary to "close the correspondence." Quotations from two other physicians, in the same issue, are illuminating as to the attitude of some panel practitioners:

> To pretend that panel and well-to-do private patients can be treated identically is to be an ostrich. Unpleasant facts must be faced. Much national health insurance practice consists of futile efforts to adapt the patient to a wrong environment by generous doses of drugs and other poisons. We are in a changing era. Public and private health are slowly merging. Perhaps in the meanwhile the national health insurance practitioner is doing useful work which will be facilitated by the gifts of hypocrisy or self deception.
>
> While it would be unfair to stigmatize the whole profession for the misdeeds of a few of its members, nevertheless there is, I believe, an increasing tendency to practice what has been described in previous letters as mechanized medicine. For this the public are in part to blame. In this aspirin-ridden age pain must be assuaged, discomfort eased forthwith and at any price, and the excuse that one may be trying to cure the case is not always received with becoming gratitude. On the other hand, there is a type of mind—present in all ages of medicine—who will choose the easier path. They have so simplified prescribing as to resemble the famous John Brown of the eighteenth century who divided all the ills of mankind into two categories: (1) the depressed, who required stimulating, and that with alcohol; (2) the overexcited, who must be soothed, and that with laudanum. Few of the modern school, one fears, are as honest as John Brown, who, believing in the efficacy of his own prescription, died of too much alcohol by day and too much laudanum by night!

1. Taylor-Thomas, F. S.: Brit. M. J. **2**: 562-563 (Sept. 12) 1936.
2. Juvenis: Brit. M. J. **2**: 650 (Sept. 26) 1936.
3. Cox, Alfred: Brit. M. J. **2**: 694 (Oct. 3) 1936.
4. Mackenzie, E. K.: Brit. M. J. **2**: 740-741 (Oct. 10) 1936.
5. Brit. M. J. **2**: 786-787 (Oct. 17) 1936.

Association News

THE ATLANTIC CITY SESSION

Symposium on Heart Disease in the Scientific Exhibit

The Committee on Scientific Exhibit has announced that an exhibit symposium on heart disease will be held at the Atlantic City session, June 7-11, 1937. The symposium, which will cover all phases of the subject, will be presented by various individuals who may have suitable material to offer and the exhibits will be open to awards. Application blanks for space may be obtained from the Director, Scientific Exhibit, 535 North Dearborn Street, Chicago.

RADIO BROADCASTS

The American Medical Association and the National Broadcasting Company are presenting the second series of dramatized health broadcasts under the title Your Health. The first broadcast in the new series, the thirty-second dramatized cooperative broadcast under the title Your Health, was given October 13. The theme for 1936-1937 differs slightly from the topic in the first series, which was "medical emergencies and how they are met." The new series is built around the central idea that "100,000 American physicians in great cities and tiny villages, who are members of the American Medical Association and of county and state medical societies, stand ready, day and night, to serve American people in sickness and in health."

The program will go out on the Blue network instead of on the Red network, as originally announced. The announcement cards that were sent out when the program was planned for the Red network can be changed simply by substituting the word "Blue" for "Red" where it occurs.

The topics are announced monthy in advance in *Hygeia*, the Health Magazine, and three weeks in advance in each issue of THE JOURNAL. The topics and speakers for the next three programs are:

December 1. "Smog." W. W. Bauer, M.D.
December 8. Heredity and Disease. Morris Fishbein, M.D.
December 15. Milk. W. W. Bauer, M.D.

The time of the broadcast is Tuesday afternoon at 4 o'clock central standard time (5 o'clock eastern time, 3 o'clock mountain time, 2 o'clock Pacific time).

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

CONNECTICUT

Society News.—Dr. Richard E. Shope, Princeton, N. J., discussed the "Newer Knowledge of Influenza" before the Yale Medical Society, November 11, in New Haven.

Dr. Ingraham Leaves State Board of Health.—Dr. A. Elizabeth Ingraham, since 1923 director of the bureau of child hygiene of the Connecticut State Department of Health, Hartford, has resigned, effective January 1, and, it is reported, will retire from active public health work.

Graduate Courses.—The Connecticut State Medical Society and the state department of health opened a course on maternal health at the Windham Community Memorial Hospital, October 6, and the Day-Kimball Hospital, Putnam, October 7. Instructors are Drs. James R. Miller, Hartford, Emerson L. Stone, Abraham Nowell Creadick, Herbert Thoms and Luther K. Musselman, all of New Haven, and Joseph H. Howard, Bridgeport. A course in pediatrics, to be given when the one in obstetrics is completed, is in charge of a committee consisting of Drs. Grover F. Powers, professor of pediatrics, Yale University School of Medicine, chairman; James Harold Root, Waterbury, and Oliver L. Stringfield, Stamford. Instructors will be selected by this committee from the membership of the state medical society. Both courses are being financed by a social security grant.

Personal.—Dr. John Homans, clinical professor of surgery, Harvard University Medical School, and surgeon to the Peter Bent Brigham Hospital, Boston, has been appointed visiting professor of surgery at Yale University School of Medicine, New Haven, and surgeon-in-chief of the New Haven Hospital during the period November 1 to June 30, 1937.——Dr. Lewis A. Sexton, for twenty years superintendent of Hartford Hospital, has retired on account of ill health. With the appointment of Dr. Wilmar Mason Allen as director of the hospital, the post of superintendent was discontinued and Dr. Sexton was designated director-emeritus.——Dr. George E. Cogan has been elected president of the Hartford Board of Health, succeeding Dr. Robert V. Boyce, who recently resigned.——Dr. Samuel Green, health officer of Southbury, has presented to the Hartford Board of Health a certificate issued by the Common Council in 1878 appointing his father, the late Dr. George S. Green, a member of the board.

DELAWARE

Society News.—Dr. Manfred S. Guttmacher, Baltimore, discussed "The Relationship of Psychiatry to the Courts" before the New Castle County Medical Society, November 17. Dr. Brooke M. Anspach, Philadelphia, discussed gynecologic conditions, October 20.

ILLINOIS

Society News.—Dr. Joseph Brennemann, Chicago, addressed the Bureau County Medical Society at Princeton, November 10, on "Pneumonia in Childhood."——At a meeting of the Will-Grundy County Medical Society, November 11, Dr. Tell Nelson spoke on the "Management of Bronchial Asthma."——Drs. Ralph A. Reis, Chicago, and Ralph P. Peairs, Normal, discussed gynecology and medical economics, respectively, before the Livingston County Medical Society, November 12.——At a meeting of the Kankakee County Medical Society, November 12, Dr. Margarete M. H. Kunde, Chicago, spoke on "Endocrine Therapy in Menstrual Disturbances."——Dr. John de J. Pemberton, Rochester, Minn., addressed the Peoria City Medical Society, November 10, on surgery of the thyroid gland.

Chicago

The Ludvig Hektoen Lecture.—Dr. Ernest W. Goodpasture, professor of pathology, Vanderbilt University School of Medicine, Nashville, Tenn., will deliver the thirteenth Ludvig Hektoen Lecture of the Frank Billings Foundation, January 22. His subject will be "Vaccinia."

Another Window Exhibit.—In the lobby window in the Annex Building of Marshall Field and Company is an exhibit on "feet" designed to show that foot disorders are frequently traced to systemic diseases and emphasizing that the family physician should be consulted before any corrective measures are introduced. Models are displayed to show that a shoe should be made to fit the foot rather than the foot to fit the shoe. There is also a model in plaster of the perfect foot of a child. This window has been given to the Chicago Medical Society, free of rental and service charges, for the display of health educational material. The material is prepared by the educational committee of the Illinois State Medical Society.

Bacteriology Reviewed.—At a meeting of the Institute of Medicine of Chicago and the Society of Medical History of Chicago, November 24, the following program was presented:

Dr. Ludvig Hektoen, Notes on the History of Bacteriology in Chicago Prior to the Organization of Bacteriologic Teaching (about 1890).
Dr. George H. Weaver, The Introduction of Bacteriology into the Medical Curriculum in Chicago.
Dr. Fred O. Tonney, The Introduction of Bacteriology into the Public Health Service in Chicago.

A paper prepared for the Society of Medical History by Dr. Jacques Holinger, before his death in 1934, was read by title: "An Incident in the Development of Antisepsis and Dr. Henry Banga's Part Therein." Dr. Peter Bassoe will deliver the presidential address before the twenty-first annual dinner and meeting of the Institute of Medicine, December 1, on "A Sketch of the Development of Psychiatry and Neurology in Chicago."

Beaumont Collection at University of Chicago.—A collection of papers and personal effects of Dr. William Beaumont has been given to the University of Chicago by the physiologist's grandson, Ethan Allen Beaumont, and his wife, of De Pere, Wis. The collection, consisting of first editions, unpublished letters, a case history, surgical instruments, photographs and a chair presented to the Beaumonts by Robert E. Lee, who once lived with them in St. Louis, was on exhibition at the university library, November 20, together with an oil portrait of Dr. Beaumont lent by Mr. A. C. Denny of Evans-

ton. During the exhibition, addresses were delivered by Robert Maynard Hutchins, president of the university, and Drs. Anton J. Carlson, Arno B. Luckhardt and Selim W. McArthur. The program, sponsored by the Friends of the Library of the University of Chicago, was planned to coincide with the one hundred and fifty-first birthday of Dr. Beaumont, November 21.

Fund for Study of Hospital Insurance.—The Rosenwald Fund has given $100,000 to the American Hospital Association to study and develop voluntary hospital insurance. The program of the association will be projected through a special committee on hospital service with C. Rufus Rorem, Ph.D., as executive director. Other members of the committee are Drs. Basil C. MacLean, Rochester, N. Y., chairman; Sigismund S. Goldwater, New York; Robin C. Buerki, Madison, Wis.; Claude W. Munger, president of the American Hospital Association, and Msgr. Maurice F. Griffin, Cleveland. According to an announcement, one phase of the work will deal with advice and consultation on existing plans and those being formed concerning actuarial data, benefits, method of organization, public relations and annual subscription rates, while a second phase will cover relations of hospital service plans to the medical profession, public welfare activities, state departments of insurance, private insurance companies, hospital administration and hospital accounting.

IOWA

Lectures for College Students.—The speakers' bureau of the Iowa State Medical Society will continue this winter its policy of providing lecturers to colleges in the state. The following program has been tentatively outlined for delivery to the freshmen at Grinnell College: The Body and Its Functions, Medical Science in the Service of Health, Upkeep and Energy Supply, Digestion and Elimination, The Use of Energy in Activities, By-Products of Activity and Energy Renewal, Body Mechanics, Thermal Regulation, Cleanliness and the Appearance, Infection and Resistance, Physical and Chemical Hazards, and Reproduction and Sex.

Regional Meetings.—The Southeastern Iowa Medical Society was addressed in Mount Pleasant, October 15, by Drs. Alfred M. Paisley, Keokuk, on eye, ear, nose and throat conditions; Leonard P. Ristine, Mount Pleasant, neurosyphilis; George B. Crow, Burlington, degenerative heart disease, and Mazyck P. Ravenel, Columbia, Mo., immunization against the infectious diseases. Dr. Lonnie A. Coffin, Farmington, delivered his address as president, and Dr. Marcus Pinson Neal, Columbia, the address of the evening on cancer as a preventable disease.——Drs. Austin C. Davis and Harry L. Smith, both of Rochester, Minn., addressed the Southwestern Iowa Postgraduate Medical Society in Atlantic, October 9, on "Clinical Significance of Basal Metabolic Rates" and "Attacks of Unconsciousness Associated with Cardiac Diseases" respectively.

Society News.—Dr. Karl A. Menninger, Topeka, Kan., discussed "The Problem of Psychological Factors in Medicine" before the Pottawattamie County Medical Society in Council Bluffs, November 16. The society met jointly with the Woodbury County Medical Society, October 12; speakers were Drs. Charles T. Maxwell, "Trends in the Treatment of Diabetes"; Wayland K. Hicks, "Vaginal Ureterolithotomy," and Peirce D. Knott, "Review of 100 Cases of Anterior Poliomyelitis with Special Reference to Therapy." All the speakers are from Sioux City.——Dr. Frank A. Evans, Pittsburgh, discussed "The Physiological Background and Treatment of Obesity and Undernutrition" before the Linn County Medical Society, November 19. Dr. Elliott P. Joslin, Boston, addressed the society, October 27, on "The Management of Diabetes." Dr. Benjamin L. Knight, Cedar Rapids, spoke on "Medical Hash and Surgical Tips."

LOUISIANA

Society News.—Dr. Bunnie M. McKoin, Monroe, discussed gonorrhea before the Tri-Parish Medical Society, October 6.——The Fourth District Medical Society was addressed, among others, in Shreveport, by Dr. Robert A. Strong, New Orleans, on vomiting in infancy.——The Orleans Parish Medical Society and the staff of Charity Hospital held a joint clinical meeting, October 26. The speakers included Drs. Stanford Chaille Jamison on "Toxic Goiter in Six-Year-Old Colored Female"; Frederick F. Boyce, "Primary Streptococcus Peritonitis"; Octave C. Cassegrain and Howard R. Mahorner, "Amebic Hepatic Abscess with Rupture in the Pleural Cavity," and Roy H. Turner, "Syphilis of the Stomach." The society was addressed November 9 by Drs. Leo N. Elson on "Treatment of Trichophytosis Interdigitalis"; Howard R. Mahorner, "Clinical Aspects of Goiter," and Francis E. LeJeune showed color motion pictures of the larynx.

MASSACHUSETTS

Cancer Decrease in 1935.—The deaths from cancer in Massachusetts decreased in 1935, the first time in ten years, according to the New York *Times*. In 1935 the death rate for men was 99.2 and for women 125.2, as compared with 107.2 and 129.4, respectively, in 1934. In 1920 the rate was 84.5 per hundred thousand of population for men and 128.6 for women.

New Commissioner of Mental Hygiene.—Dr. David L. Williams, since 1928 a member of the staff of the Veterans' Administration Facility, Bedford, has been appointed state commissioner of mental diseases to succeed Dr. Winfred Overholser. Dr. Williams graduated from Tufts College Medical School in 1906. He is 60 years of age. Dr. Overholser was named assistant commissioner of mental diseases in 1930 and commissioner in 1934.

Huge X-Ray Machine at Huntington Memorial Hospital.—A machine capable of producing 1,000,000 volt x-rays is being installed in the Huntington Memorial Hospital, Boston, newspapers report. It generates static electricity and makes possible the treatment of deep-seated malignant growths in the body. Six fast moving vertical belts carry negative electricity to the high voltage terminal in the doughnut-shaped top and on the downward path remove positive electricity from the terminal, depositing it at the grounded base. High speed electrons are thus generated at the terminal and are gathered through a vertical porcelain x-ray tube to be carried downward to a water-cooled gold target. This tube will extend through the floor of the generating room to a room below, where patients will be treated.

Society News.—Dr. Merrill Moore, Boston, discussed cases of attempted suicide in a general hospital before the Harvard Medical Society, October 27.——The Boston Pathological Society was addressed October 28 by Dr. Ernest A. Codman on "A Study of the Cases in the Registry of Bone Sarcoma of Giant Cell Tumor About the Knee."——At the annual meeting of the Massachusetts Society for Mental Hygiene in Boston, November 24, Dr. Helen MacMurchy, Toronto, Ont., spoke on "Mental Hygiene and Child Welfare."——Dr. Horace K. Sowles, Boston, will address the Pentucket Association of Physicians, December 10, on "Carcinoma of the Intestines."——M. J. Shear, U. S. Public Health Service, addressed the Suffolk District Medical Society, November 18, on "Hydrocarbons and Cancer," and Dr. Joseph C. Aub, Boston, "Cancer Research."——At a meeting of the Norfolk District Medical Society in Brighton, October 27, Drs. Thomas R. Healy, Boston, among others, discussed "Radiological Aspects of Yeast Infection of the Lungs"; Charles J. Kickham, Boston, "Recent Advances in the Treatment of Pruritus Vulvae," and John F. Casey, Boston, "Treatment of Pneumonia."——Dr. Robert A. Wilson, Brooklyn, discussed "Initiation of Respiration in Asphyxia Neonatorum" before the Obstetrical Society of Boston, October 20.

MICHIGAN

Dr. Kellogg Honored.—A dinner was held in honor of Dr. John Harvey Kellogg, Battle Creek, October 19, marking his completion of sixty years as head of the Battle Creek Sanitarium. Oct. 1, 1876, the year following his graduation from Bellevue Hospital Medical College, Dr. Kellogg took over the management of the Health Reform Institute, now known as the Battle Creek Sanitarium. He is 84 years of age.

A New Dramatic Broadcast.—A campaign to eradicate tuberculosis from Detroit was recently launched under the cooperative efforts of the Wayne County Medical Society, the Detroit Tuberculosis Sanatorium Association, the Detroit *News*, Radio Station WWJ, the Detroit Department of Health, and Paul de Kruif. One feature of the program is a weekly broadcast of "Death Fighters," a dramatic story the plot of which has been taken from the records of one of the city's hospitals. The initial presentation was given Wednesday evening November 11. The theme shows the struggle of science against the ignorance and indifference with which tuberculosis has been treated in the past. Short daily dramatic broadcasts will be offered for a time to supplement the evening weekly broadcast. The *Detroit Medical News* reports that 528 physicians have registered in the campaign, which seeks to detect tuberculosis in the incipient stage. It was pointed out that during September 47 per cent of the newly found cases were in the far advanced stage. November 18 marked the opening of a series of graduate courses on the subject at the Herman Kiefer Hospital, to be held each week.

MINNESOTA

Personal.—Dr. George B. Weiser, New Ulm, was guest of honor at a banquet recently, given by the Redwood-Brown County Medical Society, in recognition of his completion of forty-three years of practice in New Ulm. Dr. Weiser practiced fourteen years in Pennsylvania before coming to New Ulm. He graduated from Jefferson Medical College in 1879. ——Dr. Homer P. Basinger has been appointed health officer of Windom, succeeding Dr. Albert L. Perti, resigned.

MISSISSIPPI

Supervisor of Health Education Appointed.—Mrs. Eva Moore Adams has been appointed supervisor of health education, a newly created position in the state board of health. The health education division plans a careful survey of health needs and health problems in the state before adopting a definite program, which will be projected through the radio, newspapers and other mediums. The state department of health will soon begin the publication of a bulletin, which will be edited by Mrs. Adams.

MISSOURI

Director of Communicable Diseases Resigns. — Dr. Eldred K. Musson, Jefferson City, has resigned as director of the division of communicable disease control of the Missouri State Department of Health, effective October 31. He will accept a similar position with the Kansas board of health, newspapers reported.

Hospital News.—Trinity Lutheran Hospital, Kansas City, observed the thirtieth anniversary of its founding during the week of October 19. The hospital admitted its first patient Oct. 29, 1906; 225 patients were hospitalized during the first year. Of the original medical staff the following are still active: Drs. Frank J. Iuen, William C. Iuen, Hal Foster, Minford A. Hanna, Carl A. Jackson and Theodore S. Blakesley.

Society News.—The Jackson County Medical Society was addressed November 10 by Drs. Wendell Stewart, East St. Louis, Ill., on "Pneumoconiosis with Special Reference to Silicosis," and Orville Harry Brown, Phoenix, Ariz., "What Every Physician Should Know About Clinical Allergy."—— Drs. Franz J. Arzt and Garold V. Stryker, St. Louis, addressed the Marion-Ralls County Medical Society in Hannibal, October 9, on "Treatment of Subacute Pelvic Inflammation" and "Skin Signs of Hypovitaminosis" respectively.——The St. Louis Medical Society was addressed, November 10, by Drs. Julius Jensen and Carl R. Wegner on "Significance of High Blood Pressure in Pregnancy," and Jonas Curtis Lyter, "Angina Pectoris of Effort and Associated Phenomena."

Dr. Coughlin Honored. — Dr. William T. Coughlin, St. Louis, head of the department of surgery, St. Louis University School of Medicine, was guest of honor at a dinner given by the school, November 12, in recognition of his completion of twenty-five years' service on the faculty. Dr. Coughlin graduated from Washington University School of Medicine, St. Louis, in 1901, serving on the faculty there from 1901 to 1911, when he went to the St. Louis University School of Medicine as assistant professor of surgery. He was made head of the department in 1920. He was presented with a volume of letters of congratulation, and a collection of books is to be assembled at the university library in his honor. Other guests of honor at the dinner who have also completed twenty-five years' service on the faculty were Drs. Carl Barck, Louis C. Boisliniere, Jules M. Brady, Edward P. Buddy, Cyrus E. Burford, John McH. Dean, William P. Glennon, William W. Graves, Alexander E. Horwitz, Joseph M. Keller, William E. Leighton, Bransford Lewis, Augustin P. Munsch, Louis Rassieur, Carroll Smith, Percy H. Swahlen, Frank J. Tainter, Ralph L. Thompson and Hillel Unterberg. Rev. Alphonse M. Schwitalla, S.J., dean of the school, presided, and Dr. Loyal Davis, head of the department of surgery, Northwestern University Medical School, Chicago, spoke on "Early Contributions of the Middle West to Surgery." The president of the university, Rev. Robert S. Johnston, also spoke.

NEW JERSEY

Society News.—Dr. Oliver H. Perry Pepper, Philadelphia, addressed the Atlantic County Medical Society, Atlantic City, November 13, on "Diseases of the Esophagus from the Viewpoint of the Internist."——Dr. Warren B. Davis, Philadelphia, addressed the Hudson County Medical Society, Jersey City, November 4, on "Congenital and Acquired Deformities of the Face and Their Surgical Repair."——Dr. Arthur F. Coca, Pearl River, N. Y., addressed the Bergen County Medical Society, November 10, on "The Newer Antibodies."

NEW YORK

Educational Campaign on Cancer. — The Westchester Cancer Committee conducted an educational campaign during October, concentrating on cancer of the breast. Pamphlets on this form of the disease were distributed through clubs and fraternal organizations and a special feature was a dinner attended by about 125 teachers of biology and science, superintendents of schools and physicians. A Westchester Institute of Science was organized to meet twice a year to hear cancer authorities and relay their messages to high school and college students. Clarence C. Little, Sc.D., director of the American Society for the Control of Cancer, Bar Harbor, Maine, and Dr. George T. Pack, New York, were the speakers at the dinner.

Conference at University of Rochester.—The University of Rochester School of Medicine and Dentistry presented a postgraduate medical conference, November 5-7, to alumni and other physicians of that section of the state. The medical faculty conducted in Strong Memorial Hospital clinical demonstrations, outpatient clinics, clinical pathologic conferences, bedside rounds and operative clinics. There was a dinner Friday evening November 6 at which Dr. Floyd S. Winslow, Rochester, president of the Medical Society of the State of New York, was toastmaster. Later the guests attended the Eastman Memorial Lecture delivered by Dr. Russell L. Haden, Cleveland, on "Clinical Manifestations of Nutritional Deficiency Diseases."

Society News.—Dr. Elmer B. Freeman, Baltimore, addressed the Glens Falls Academy of Medicine, October 16, on "The Practical Value of Special Diagnostic Methods in the Study of Digestive Diseases."——Dr. Edward C. Reifenstein, Syracuse, addressed the Onondaga Medical Society and the Syracuse Academy of Medicine, November 17, on "The Significance of Heart Murmurs" and Dr. Tracy L. Bryant reported two cases of gas gangrene.——Dr. William D. Johnson, Batavia, addressed the Oswego County Medical Society, Oswego, November 12, on "Acute Diseases of the Abdomen."—— Dr. Gershom J. Thompson, Rochester, Minn., among others, addressed the Western New York and Ontario Urological Society, which met at the Robert Packer Hospital, Sayre, Pa., October 10, on transurethral prostatectomy.

New York City

Hospital News.—The family of the late Dr. Max Rosenthal recently made a gift of $5,000 to Sydenham Hospital for a fellowship fund to finance research in medical problems. Announcement of the gift was made at the unveiling of a bronze tablet to the memory of Dr. Rosenthal, who died April 3. He was a founder of the hospital and formerly president of the medical board.——Dr. George T. Pack lectured at a clinical conference of the Memorial Hospital of Queens, November 24, on recent advances in cancer research.

Medical-Dental Joint Meeting.—The sixth annual Medical-Dental Convention arranged by the Joint Committee of the Organized Medical and Dental Professions of New York will be held at the Hotel Pennsylvania December 7. The morning speakers will be Dr. Samuel Feldman, on "Diseases of the Oral Cavity of Medical and Dental Interest" and Bernhard W. Weinberger, D.D.S., "Medical Problems in Orthodontia." The afternoon session will be a clinical meeting with presentation of patients. In the evening Dr. Hayes E. Martin will address the assembly on "The Responsibility of the Dental Profession in the Early Diagnosis of Intra-Oral Cancer."

Eyeglasses for Persons on Relief.—A clinic operated by four ophthalmologists has been placed in service by the Emergency Relief Bureau to expedite the distribution of eyeglasses to persons on relief. It is estimated that about 11,000 school children need glasses and that many adults have missed opportunities for reemployment for lack of them. Under the new plan the eye clinic will rotate among eight district relief offices covering all five boroughs. Relief recipients are given appointments at the nearest offices, thus lightening pressure on hospital clinics and reducing the delay in distribution of the glasses from five weeks to one week. The bureau is distributing about 200 pairs of glasses a week at a cost of $2.11 a pair. It is also filling prescriptions for home relief recipients who have been examined by ophthalmologists in public and private hospitals, provided the prescriptions fall within the bureau's eligibility rules as to vision and employability.

Society News.—At a meeting of the New York Gastroenterological Association, November 17, the speakers were Drs. Henry A. Rafsky, on "A Study of the Glycemic Response in Patients with Biliary Tract Disease"; Reuben Ottenberg and

Ralph Colp, "Diagnosis of Surgical Jaundice," and Eilif C. Hanssen, "The Present Status of the Typhoid Carrier."——A symposium on sterilization was presented at a meeting of the section of obstetrics and gynecology of the New York Academy of Medicine, November 24, by Drs. Benjamin P. Watson, Eliot Bishop, Ira I. Kaplan, John H. Wyckoff and Foster Kennedy; Marie E. Kopp, Ph.D., and William J. McWilliams, counsel for the National Committee on Maternal Health.—— Dr. Irving Schwartz addressed the New York Roentgen Society, November 16, on "Roentgenology of the Sinuses and Skull." ——Drs. Boris M. Fried and Wolfgang Grethmann addressed the New York Pathological Society, November 19, on "The 'Primary Complex'—Initial Lesion in the Childhood Type of Tuberculosis" and "Pathogenesis of Tuberculosis as a Systemic Disease" respectively.—— Drs. Joseph Felsen and Albert A. Berg addressed the Medical Society of the County of Kings, November 17, on chronic bacillary dysentery.

PENNSYLVANIA

Society News.—Dr. Frederick J. Bishop, Scranton, addressed the Northampton County Medical Society, Easton, November 20, on "Closer Cooperation Between Professional Men."—— Dr. John B. Lownes, Philadelphia, addressed the Montgomery County Medical Society, Norristown, November 4, on problems in urology.

Philadelphia

Society News.—Dr. Nathan Chandler Foot, New York, was the guest speaker at a meeting of the Pathological Society of Philadelphia, November 12; his subject was "A Criticism of Laboratory Routine in Modern Institutions of Pathology."——Dr. Ralph M. Tyson, Dr. Henry Harris Perlman and Earl A. Schrader, M.S., among other speakers, addressed the Philadelphia Pediatric Society, November 10, on "Drugs Transmitted Through Breast Milk: Part I. A Study of Laxatives."——Dr. Linwood D. Keyser, Roanoke, Va., addressed the Philadelphia Urological Society, October 26, on "Pathogenesis of Urinary Calculi; Experimental and Clinical Survey."

Changes at College of Pharmacy.—Charles H. La Wall, Phar.D., for many years dean of pharmacy and formerly professor of theory and practice of pharmacy at the Philadelphia College of Pharmacy and Science, has been appointed professor of pharmacy. He retains the deanship. Ivor Griffith, Ph.M., associate professor of pharmacy, has been made assistant dean of pharmacy and professor of theory and practice of pharmacy. Arthur Osol, Ph.D., has been appointed director of chemical laboratories to succeed Prof. Frank X. Moerk, Ph.M., who became emeritus director. Adley B. Nichols, Phar.D., has been advanced to the rank of associate professor of pharmacy; John N. McDonnell, Sc.D., and Linwood F. Tice, M.S., have been made assistant professors of pharmacy, and Joseph W. E. Harrisson, Phar.D., has become assistant director of biologic assaying.

RHODE ISLAND

Society News.—Dr. George W. Waterman, Providence, addressed the Pawtucket Medical Association, October 15, on "Pituitrin—Its Uses and Abuses."——At a meeting of the Rhode Island Medicolegal Society, October 29, Joseph H. Hagan, chief of the division of probation and parole, state department of public welfare, spoke on "Understanding the Delinquent."

Clinic Day.—Memorial Hospital, Pawtucket, held its annual clinic day November 4. Clinics were conducted by the staff in the morning and the following program of addresses was presented in the afternoon:

Dr. Claude F. Dixon, Rochester, Minn., Surgical Management of Carcinoma of the Colon.
Dr. John Eiman, Abington, Pa., Observations on Hypochloremia and Hyperchloremia.
Dr. George M. Piersol, Philadelphia, Importance of Restoring and Maintaining Proper Chemical Balance in Chronic Renal Conditions.
Dr. Henry L. Bockus, Philadelphia, Regional Ileitis and Ileocolitis.
Dr. Harry B. Wilmer, Philadelphia, Glucose Tolerance and Metabolism in the Allergic Individual.
Dr. William D. Stroud, Philadelphia, Result of Five Years' Study at Pennsylvania Hospital of Various Digitalis Preparations and the Present Attitude Toward Digitalis in the Treatment of Cardiovascular Disease.

TENNESSEE

Clinical Meeting in Chattanooga.—A clinical congress was held by the Chattanooga and Hamilton County Medical Society October 15 at the Hotel Patten in Chattanooga. The guest speakers were Drs. Ray M. Balyeat, Oklahoma City; Hal M. Davison, Atlanta; Barney Brooks, Nashville, and Wilson L. Williamson, Memphis, president of the Tennessee State Medical Association.

Society News.—Dr. Claude C. Coleman, Richmond, Va., was the guest speaker at a meeting of the East Tennessee Medical Association in Cleveland, October 6, on "Diagnosis and Treatment of Brain Tumors." Among other speakers were Drs. Edward T. Newell, Chattanooga, on "Fractures and Dislocations of the Spinal Column"; Milton Smith Lewis, Nashville, "Treatment of Eclampsia," and Estill L. Caudill, Elizabethton, president of the society, "Acute Intestinal Obstruction."

VERMONT

Society News.—Dr. Gregory Zilboorg, New York, addressed the New England Society of Psychiatry at its fall meeting in Brattleboro, October 8, on "Borderlines of Knowledge in Present-Day Psychiatry."

WISCONSIN

Dr. Sleyster Honored.—The Medical Society of Milwaukee County sponsored a dinner to Dr. Rock Sleyster, Wauwatosa, Chairman of the Board of Trustees of the American Medical Association, November 14, at the Wisconsin Club, Milwaukee, in honor of his thirty-three years of service to organized medicine. Dr. Arthur J. Patek, Milwaukee, was toastmaster and the speakers were Drs. Charles Gordon Heyd, New York, President of the American Medical Association; Olin West, Chicago, Secretary and General Manager of the Association; Morris Fishbein, Chicago, Editor of THE JOURNAL; Stephen E. Gavin, Fond du Lac, president of the State Medical Society of Wisconsin; Eben J. Carey, dean, Marquette University School of Medicine, Milwaukee; Arthur W. Rogers, Oconomowoc; Chester M. Echols, president of the Medical Society of Milwaukee County; J. Gurney Taylor, Milwaukee; the Rev. Anthony F. Berens, S.J., regent of Marquette University School of Medicine, and Dr. Sleyster. In 1903 Dr. Sleyster became secretary of the Calumet County Medical Society, continuing six years. He was elected assistant secretary of the State Medical Society of Wisconsin in 1910 and secretary in 1914. He remained as secretary until 1923 and was elected president in 1924. Since 1925 he has been treasurer of the society. From 1918 to 1923 Dr. Sleyster was editor of the *Wisconsin Medical Journal.* From 1915 to 1926 he served as delegate to the American Medical Association and the last four years of that period was vice speaker of the House of Delegates. He has been a Trustee since 1926 and chairman of the Board since 1935. Dr. Sleyster was graduated from the University of Illinois College of Medicine, Chicago, 1902. He is medical director of the Milwaukee Sanitarium, Wauwatosa, a fellow of the American College of Physicians, a member of the American Psychiatric Association, the Association for Research in Nervous and Mental Diseases and the Central Neuropsychiatric Association.

GENERAL

Lectureship in Honor of C. Jeff Miller.—The Southeastern Surgical Congress has established a lectureship in honor of the late Dr. C. Jeff Miller, New Orleans, who was president of the congress at the time of his death. The lecture will be given annually during the regular convention of the congress. Dr. William D. Haggard, professor of clinical surgery, Vanderbilt University School of Medicine, Nashville, will deliver the first lecture in Louisville, March 8, 1937.

The Jacobi Fellowship.—The Women's Medical Association of the City of New York offers the Mary Putnam Jacobi Fellowship of $1,000 for one year for postgraduate work in the medical sciences. The fellowship is open to any woman graduate of an approved medical school. The recipient must give full time to the study of a special problem, preferably abroad; if the recipient is not a resident of the United States, the study should be made in the United States. Applications for 1937-1938 should be filed with the chairman of the committee on or before April 1, 1937. A report for publication will be required at the completion of the fellowship. The chairman of the committee is Dr. Annie S. Daniel, New York Infirmary, 321 East Fifteenth Street, New York.

Society News.—Dr. Charles V. Craster, Newark, N. J., was chosen president of the International Society of Medical Health Officers at its meeting in New Orleans, October 21. Drs. Eugene L. Bishop, Knoxville, Tenn., and A. G. Brito, Mexico City, were elected vice presidents and Dr. Francis E. Harrington, Minneapolis, was reelected secretary.——Dr. Joseph C. Brugman, Seattle, was elected president of the North Pacific Orthopedic Society at its annual meeting in Spokane, Wash., in September. Dr. Edward A. LeCocq, Seattle, was elected secretary.—— The Pacific Northwest Society of Pathologists held its semiannual meeting in Spokane, Wash., October 10.

The subject discussed was "Lesions of the Kidney." Dr. Mathew M. Patton, Spokane, was elected president and Dr. James D. Edgar, Spokane, secretary.

Bequests and Donations.—The following bequests and donations have recently been announced:

Bridgeport Hospital, Bridgeport, Conn., $25,000 for the establishment of a free bed for indigent residents of Fairfield.

Chambersburg Hospital, Chambersburg, Pa., $2,500 by the will of the late M. C. Kennedy.

Bronx and Beth Israel hospitals, New York, $10,000 each, and Montefiore Hospital, New York, $5,000 by the will of I. Miller.

New York Orthopedic Dispensary and Hospital, $7,000 in trust bequeathed by Ella Lyon Dayan.

St. John's Riverside Hospital, $50,000, and the Yonkers General Hospital, $25,000, Yonkers, N. Y., by the will of Miss Mary Colgate.

Children's Hospital, Cincinnati, a residuary estate estimated at $250,000 by the will of Mrs. Annie L. Dana.

Mount Sinai Hospital, New York, $50,000 and New York Medical College and Flower Hospital $10,000 from the estate of the late Charles Strauss.

Philadelphia Children's Hospital, $10,000 by the will of the late Howard Fuguet.

New York Post-Graduate Medical School and Hospital and Babies' Hospital, New York, each one sixth of an estate estimated at about $2,000,000 left by Miss Gertrude S. Thomas; she also bequeathed $5,000 to the New York Eye and Ear Infirmary.

National Society for the Prevention of Blindness.—The annual conference of the National Society for the Prevention of Blindness will be held at the Deshler-Wallick Hotel, Columbus, Ohio, December 3-5. Sessions will be devoted to a discussion of saving eyesight in industry, eye health in relation to social work, eye health of college students, the nurses' approach to eye health, teacher education in eye health and sightsaving classes in the public schools. There will be a forum on "Rehabilitation vs. Relief," with Lewis H. Carris, New York, managing director of the society, as discussion leader. Speakers will include:

Dr. Carl E. Rice, consultant, Social Security Board, Washington, D. C.

Dr. Ruth Boynton, University of Minnesota Medical School, Minneapolis.

C. Edith Kerby, statistician, National Society for the Prevention of Blindness, New York.

Dr. Claude S. Perry, Columbus, Ohio.

There will be a dinner meeting sponsored by the Columbus Academy of Medicine, with Dr. Edward Jackson, emeritus professor of ophthalmology, University of Colorado School of Medicine, Denver, as the speaker. His subject will be "Guarding the Sight of School Children." Audrey M. Hayden, executive secretary of the Illinois Society for the Prevention of Blindness, will address a luncheon meeting on "Selling Sight-Saving Classes to the Public." The annual meeting of the national society will be held at the Russell Sage Foundation Building, New York, December 11.

Changes in Status of Licensure.—The California Board of Medical Examiners recently reported the following:

Dr. Herman Gordon Bayless, Los Angeles, placed on probation for five years, during which time he shall not have or apply for a narcotic permit or have narcotics in his possession.

Dr. Leman Dow Cruice, La Mesa, restored to practice but not permitted possession of a federal narcotic tax stamp or the use of narcotics.

Dr. Milton M. Kay, Shafter, placed on probation for five years, during which time he shall not apply for or have a federal narcotic tax stamp or have narcotics in his possession.

Dr. William I. Kinsley, San Diego, license restored but not permitted to apply for a federal narcotic tax stamp or the use of narcotics.

Dr. Frederick H. C. Olberg, Redding, placed on probation for five years during which time he shall not have or apply for a federal narcotic tax stamp nor have narcotics in his possession.

Dr. William B. Payton, Riverside, placed on probation for five years, during which time he shall not apply for or have a federal narcotic tax stamp or have narcotics in his possession.

The Massachusetts Board of Registration in Medicine announces the following:

Dr. Frank S. Parsons, Dorchester, license restored; it had been revoked March 10, 1927.

Dr. Percy W. Carr, River Street, Boston, license restored; it had been revoked April 26, 1934.

The New Mexico Board of Medical Examiners recently reported the following action:

Dr. John Lawrence Kirby, whose last known address was Shreveport, La., license restored October 14; it had been revoked Oct. 14, 1935, for narcotic violations.

The New York State Board of Medical Examiners reported the following action, taken September 21:

Dr. James Morris Hackett, Leonia, N. J., license revoked because of his conviction of a felony.

The State Board of Medical Education and Licensure of Pennsylvania recently reported the following action:

Dr. Richard Paul Jahnig, Reading, license restored October 23; it was suspended April 16 because of narcotic violations.

The State of West Virginia Public Health Council recently reported the following:

Dr. John B. Rosier, Salem, license revoked October 14, because of narcotic violation.

Dr. Elihugh H. Kile, Flatwoods, license restored; it had been revoked March 13, 1934, for narcotic violations.

FOREIGN

Personal.—Dr. John Mellanby, Waynflete professor of physiology at the University of Oxford, and Lord Balfour of Burleigh have been appointed to the Medical Research Council in succession to Prof. Edgar D. Adrian and the Marquess of Linlithgow, who retired September 30. Lord Balfour of Burleigh has been made chairman.

Congress on Military Medicine.—Thirty nations were represented at the sixth session of the International Office of Documentation of Military Medicine in Geneva, Switzerland, October 12-14. Among the subjects discussed were comparative studies of medical service units in various countries; field instruction of medical units in the Swiss army; the psychologic background of the aviator; principles and means of evacuation in a combat division; panic as a war phenomenon; psychiatry in an army. The session adopted a resolution urging revision of the laws of war, which is now the subject of study by a commission created by the permanent committee of the International Congress of Military Medicine and Pharmacy (THE JOURNAL, May 23, p. 1828). The next meeting of the International Office of Documentation will be held during the ninth International Congress of Military Medicine and Pharmacy in Bucarest in June 1937.

Government Services

Report of Food and Drug Administration

Staple drugs showed a 91 per cent conformity to official standards of strength and purity during the past year, according to the annual report of the Food and Drug Administration. A survey carried out in the spring of this year, in which the output of 399 manufacturers was sampled, showed that in 2,246 containers analyzed, only twenty-four were below the standard of the U. S. Pharmacopeia. Unofficial drugs showed a greater violation; of 2,626 samples examined (the output of 374 manufacturers), 171 departed from the composition or potency noted on their labels.

An unusual problem in the work of the administration this year was disposition of food and drugs soaked by polluted water during the floods of last winter and spring, in which the department cooperated with federal, state and local officials. The report states that in 140 towns and cities visited by federal inspectors 1,385 carloads of water-soaked foods and drugs were kept under surveillance. Seizure under federal law was necessary in only ten instances, involving forty-one tons of stock feeds, coffee, butter, shortening, candy, cheese, breakfast foods and flour. It was estimated that about 50,000 tons of food and drugs were destroyed in the flood area.

Improvement was reported in conformity to limits established for poisonous spray residues on fruits and vegetables. The arsenic tolerance was almost universally met and most foods were found to be practically free from lead, except for accidental and preventable contamination. In 66,632 samples taken, only 146 seizures were necessary as compared with 334 in the previous fiscal year.

Canned salmon, previously showing continual improvement, was exceptionally bad, the report says. Thirteen hundred samples were taken and 294,000 shipping cases were seized. Only five seizures were made of canned tuna fish and canned mackerel was of uniformly high quality. Importations of cocoa beans, nuts, spice seeds, dates and figs were carefully supervised during the year, more than 20 million pounds being denied entry because of dirt or decomposition.

Substitution of "tea seed oil" for olive oil was detected by means of a chemical test developed by an administration chemist and 13,658 gallons of the so-called olive oil was rounded up.

A comparable fraud in the substitution of isopropyl alcohol for ethyl alcohol in "rubbing alcohol" was also run down during the year. Twenty thousand bottles were seized under a provision of the law that isopropyl alcohol preparations intended for external bodily use must show the exact nature of the article without accompanying words or trade names that would tend to confuse the product with ethyl alcohol, it was stated in the report.

During the year the administration found illegal 2,683 samples from interstate shipments of foods and drugs. Of these 2,092 were of foods and stock feeds and 591 medical and other drug preparations.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Oct. 17, 1936.

The Importance of Poise in a Mad Europe

In his presidential address to the Royal Medical Society of Edinburgh, Lord Horder dealt with some of the social problems of the day from the physician's standpoint and even touched on international ones. He emphasized the view that physicians could make useful contributions toward happiness and so indirectly toward health. There was a considerable overlap between these two things. He was not sure that they could do much more than had been done along the more hackneyed lines of preventive medicine, which had made good in the main. We lived longer and more healthily than we ever did. But that was not all. When he arrived at New York a few months ago, representatives of the press crowded into his cabin and asked him whether medicine had done anything recently (meaning during the past few days) to prolong life. He replied: "Surely we live long enough, isn't the problem how to live more happily?" In this the physician could help in several ways by his special knowledge and by his personal influence. There was the ministry of health and the department of health. Surely there could be a ministry and a department of public happiness. With such an ideal ministry of happiness would not the political hyperpyrexia of recent days in the east end of London (produced by a facist demonstration) and some states of political and social stress in other places be its concern rather than that of the home office (the police)? There was too much canned food for the mind.

However, whether through ministries and departments of health or by other corroborate means, the medical profession must take its share in the work. The times were critical. They were made so by the sense of imminent risk of a conflagration which a few cool heads were doing their utmost to avert. If we failed to keep our poise as a nation we might precipitate the pandemonium. Such a failure would be largely because we had too long neglected the simple factor of public happiness through the avenue of public health. For the physician there could be no left or right. For him there was expert knowledge, a rooted adherence to truth and horse sense. That British mixture was their equipment in what was perhaps the most lethal fight they had ever, as individuals and as a body, had to face, the fight for stability of mind and of body in the interest not only of national existence but of the existence of civilization. The position facing us was appalling.

He would state the desiderata in terms that were clear, however crude: 1. Enough of the right food in the belly. But it was no use telling people to drink more milk if they could not get it. At present milk costs 4 cents a gallon for making walking-stick handles and 20 cents a gallon for human food. The problem of distribution must be tackled. 2. Easy access to fresh air. 3. Shelter at a rent that left something to buy food. 4. Leisure for play, and that might lead to thinking, even high thinking. 5. Noise control.

The answer to the question why they should try to secure physical health and happiness of the people was in order that we should preserve our mental poise while large sections of humanity were losing it. This mental poise, if only we could keep it, might save civilization. But if we developed national hysteria or national hypochondriasis, this unique opportunity would be lost forever. We were told that other nations had ideals and that these stimulated them to fitness and efficiency. But we British had an ideal too that was more dearly cherished by the universal heart of mankind and therefore had more permanence than any determined by a merely temporary objective. The deep and fundamental note in our ideal was freedom. Would that a voice oracular might peal and waken us to the realization that to maintain this ideal we must be happy.

The Mental Health Service

In its annual report, the board of control (the body appointed by government to control the care of mental patients) notes with satisfaction the increased proportion of patients admitted to mental hospitals without certification. The steady increase in the number of voluntary patients affords a striking refutation of the criticism, often made, that no one would enter the hospitals except by compulsion. Before the recent regulation which admits voluntary patients, admission was only on certification of insanity by two physicians. The stigma of this was so objectionable to the family of the patient that it was avoided as long as possible, with the result that the opportunity for hospital treatment in the early stage was lost.

Outpatient centers are increasing in number, but in some areas the intervals between sessions are much too long. The remedy for this is to increase the staff, not to decrease the number of sessions, for persons in the incipient stages of mental trouble are "shy creatures" and will not readily give their confidence to a physician who can see them only once a month. It is pointed out that outpatient centers cost little to maintain and are the best investment a visiting committee can make, for they will save many patients from the need of inpatient treatment.

The necessity for the appointment of trained social workers to assist the medical staff of outpatient centers and mental hospitals, and their value as links between the medical staff and the patients' homes, in relation both to treatment and to after-care, is emphasized. The diet in mental hospitals is generally good in quality and adequate in quantity, but regret is expressed that no experiment has yet been made with the cafeteria system, adopted in the United States, with a view to making the meals more attractive and improving the service. The essence of this system is that on entering the dining room the patient is given a plate which he takes to the service counter, where he is offered a choice of dishes. It might be supposed that it would lead to waste to offer patients a choice of food, but in practice it has been found that, with a little experience, the relative popularity of different dishes can be estimated. The board deplores the fact that in some mental hospitals clothing of a definitely institutional type continues to be supplied even to the better behaved women patients.

Jan. 1, 1936, the number of persons suffering from mental disorder—voluntary, temporary and certified patients—was 153,771, an increase of 1,682 over the previous year. The average annual increase for the five years that ended in 1935 was 1,714. The increased number of notified patients does not imply an increase of insanity in the general population. Of the total admissions to public mental hospitals, 24.1 were voluntary, 5.2 temporary and 70.7 certified. The increasing advantage taken of the recent introduction of voluntary admission is shown by the fact that the percentage in 1931 was only 7.1.

The Automatic Control of Radium

At the Westminster Hospital, where special attention has been given to radium therapy for some time, an important advance in technic has been made. The new installation incorporates a system of distant control for the better protection of operators and has allowed larger "bombs" to be used. Additional radium has been acquired to give effect to the conclusion earlier reached by the surgeons in charge of the radiotherapy department that deeper penetration can be obtained by removing the radium to a greater distance from the point of application. Four grams of radium, valued at about $200,000, is used and is carried alternately by two bombs. By a system of auto-

matic electrical control the radium in its container can be lifted from a leaden safe into one of the bombs and swung into position over the patient. The electrical switchboard is situated 14 feet from the patient's couch. The two bombs and the radium container are made of a heavy ray-proof metallic compound recently invented. The installation, which has involved months of experimental construction and the use of expensive metals and special tools, has cost about $4,000 apart from the radium.

Improved Plague Vaccine

As the result of recent discoveries at the Haffkine Institute of Bombay, a vaccine has been produced for the treatment of plague of which the protective power is increased thirtyfold. Work has been going on at the institute on the measurement of the virulence of plague cultures, and biologic methods for the standardization of plague vaccine have been evolved. This is claimed to be the first successful standardization of bacterial antigen. With a serum of the great potency thus achieved, from 70 to 80 per cent of experimentally infected animals can be saved, whereas failure has hitherto attended the use of the serums on the market. Trials in the use of the new serum in human cases are now in progress. Preliminary reports show that while the mortality in untreated cases is 76 per cent, that in treated cases has been reduced to 18 per cent.

Experiment with Substandard Army Recruits

An experiment with substandard army recruits is being watched with considerable interest and, if successful, its scope will probably be extended. At present thirty-two men, all of whom in one way or another did not reach the necessary standard on enlistment, have reached the twelfth day of a course that is to last three months. Yet already careful training, proper food and specialized exercises have effected a marked improvement. They are more mentally alert, they have put on weight, and their chest measurements have increased. The average increase in weight is 2½ pounds (1,135 Gm.). It is expected that if the present rate of progress continues the great majority of the recruits will be passed as fit for service at the end of the course. Nine of the men failed to reach the required chest measurement. One man who had been a kitchen porter had no chest expansion whatever. He has shown the greatest increase, 1 inch, while the average increase is half an inch. The normal daily ration allowance has been supplemented by extra milk and fresh fruit. Special games, physical training, remedial exercises and education figure in the course, with long walks in the country on Sundays.

The Smoke Evil

Presiding at the conference of the National Smoke Abatement Society, Sir George Newman, formerly chief medical officer of the ministry of health, said that he had always been impressed with the backwardness of this country in not controlling the smoke nuisance. We were very backward compared with our neighbors across the channel. Sir Leonard Hill (the physiologist) said that we had pure water and good drainage and now we must have clean air. It was far less costly to prevent than to cure disease. We lost the genial warmth and light of the sun by our dirty air. Exposure of the skin to sunlight increased the disease-resisting powers of the body, but our smoke-polluted cities interfered with this. Sir Henry Gauvain, the pioneer in this country of the open-air treatment of tuberculosis, spoke on "Light and Clean Air in Relation to Surgical Tuberculosis." He said that it was common fallacy to imagine that where sun treatment was indicated the patient should be sent to a very sunny locality where there was intense and continuous sun of high actinic value. For very strong, dark adults capable of responding to intense exposure, that was commendable. But for the majority of sick people initial weak stimulation was preferable. There were few countries where sun treatment might be practiced under more ideal conditions in the spring and summer than in the south of England, where abundant sunshine for therapeutic purposes was available, sometimes largely in excess of the patient's need.

Medical School at Oxford

Lord Nuffield, automobile manufacturer, has made the munificent offer of $6,250,000 to Oxford University for the establishment of a graduate medical school, which has been gratefully accepted. He has previously shown great interest in medical work by his benefactions to hospitals and otherwise. By discussion with the leaders of the medical profession he is well acquainted with the problems of practice and of research. He realizes that progress in medical science is reaching a stage at which it is desirable for those who work in the field of research to undergo a period of postgraduate training in modern methods of investigation, to keep in close touch with the sciences ancillary to medicine and to pursue their studies unhampered by the cares of private practice and routine teaching. Thence it is an easy step to the conception that a postgraduate medical school in a university town, in which all the scientific departments are within easy reach of the hospitals and in which the coordination of health services are established, would improve the facilities of those engaged in clinical work, whether institutional or that of general practice. In his presidential address at the recent meeting of the British Medical Association at Oxord, Sir Farquhar Buzzard spoke of the development of such a school at Oxford as an ambitious dream, thus filling the one conspicuous gap in the system of medical services. There is already at Oxford an Institute of Medical Research on a small scale, which Lord Nuffield founded. It is largely due to him that the Oxford hospitals have been reequipped and enlarged and are now provided with 650 beds. It is a condition of his offer that administration of the funds should provide for harmonious cooperation between the university and the hospitals.

The basis of Lord Nuffield's proposal is that the university, offering an environment more favorable to research than a big training hospital, should widen the scope of its medical school and of the Nuffield Institute for Medical Research for the purpose indicated. This would involve the establishment of senior posts not subject to the distractions of private practice, under whose direction there would be a body of salaried clinical assistants and house officers selected for their aptitude for research. The university would establish clinical departments of medicine, surgery, obstetrics and gynecology as well as of such other departments as may from time to time seem desirable. Each department would be under the control of a full time university professor, for whose payment the scheme provides.

The Physician as a Teacher

In an address to the students of Guy's Hospital, Lord Dawson said that nothing was widening the physician's horizon more than the development of preventive medicine. Physicians no longer looked after a cloistered class of sick people withdrawn from the community. Today they were more concerned with the children in the schools and the workers in the factories. More and more the physician would come to have a teaching function. Teaching how to keep well would come within his province, and the medical and teaching professions were likely to come closer and closer together. The physician could not aid those who wished to lead healthy lives unless there were suitable surroundings in which to work. It would fall to the physicians of the future to take a larger part in the life of the community and in the policy that concerned its health and vigor. Our present piecemeal social policy had no coherent purpose and was too much shaped by expediency. There was not behind it the study of scientific law and biologic facts on which alone

the health of the people could be founded. Falling death rates were matters for congratulation only so far as they denoted the preservation of people healthy enough to enjoy life and effective enough to be sound workers and sound players. Aside from this the benefits were doubtful.

PARIS

(From Our Regular Correspondent)

Oct. 20, 1936.

Nephrosis and Nephritis

At recent meetings of the Société médicale des hôpitaux a number of cases were reported which reflect the views of prominent internists here on nephrosis and nephritis. At the June 12 meeting, Pasteur Vallery-Radot and his associates reported a case of "lipoid nephrosis," which had been followed for four years. During the first two years, the clinical picture was that of a pure lipoid nephrosis, but even during this period of observation the presence of red blood cells in the urinary sediment had obliged the authors to alter the diagnosis so as to read "nephritis with superadded humoral syndrome of lipoid nephrosis." The subsequent evolution of the symptoms and signs confirmed this diagnosis. The lipoid nephrosis syndrome receded and the nephritis with uremic symptoms and hypertension replaced the original clinical picture of a lipoid nephrosis until the fatal termination of the case. At necropsy only the histologic changes of an ordinary chronic nephritis were to be found; hence the case was interpreted as a "nephritis with humoral syndrome of a lipoid nephrosis." The authors maintained that the case shows the lack of justification in making a distinction between a lipoid nephrosis and a nephritis. In the discussion, Cathala took exception to this opinion. He believed that a lipoid nephrosis existed as a clinical entity both in adults and in children. He cited the case of a woman, aged 28, who had an anasarca with marked albuminuria but no red cells in the urine. The blood examination was also characteristic of a lipoid nephrosis. There had been two similar transitory attacks, one at the age of 2 and the other at 18. Cathala was of the opinion that a lipoid nephrosis constitutes a special clinical entity that must be considered apart from the usual forms of nephritis. In closing the discussion, Pasteur Vallery-Radot maintained that lipoid nephrosis is rare and that it is necessary to follow a case for a prolonged period before one can say positively that no involvement of the kidney exists. If this should be done, it would soon become evident that the case was one of nephritis with a special syndrome.

A second paper on subacute nephritis due to acute lead poisoning was also read by Pasteur Vallery-Radot and his associates. The patient was a woman, aged 21, who was admitted to the hospital on account of severe abdominal pain. She gave the history of having taken 30 Gm. of a lead preparation as an abortifacient. After a primary phase, of which the principal features were vomiting, abdominal pain and stomatitis, the symptoms of a hepatonephritis appeared. The urine contained albumin and red cells. There was also a marked oliguria and high blood urea. The hepatic involvement was characterized by a subicterus and the presence of urobilin and bile salts in the urine. Sixteen months later the examination showed that a chronic nephritis was in process of development.

Cases of nephritis due to acute lead poisoning are comparatively rare. The majority of the patients die of an acute nephritis; hence one has seldom the opportunity of observing a case developing into a chronic nephritis.

Lipoid Nephrosis Following Gold Salt Treatment

At the June 19 meeting of the Société médicale des hôpitaux the case was reported of a woman, aged 27, to whom two series of injections of gold salts had been given for a severe progressive rheumatism. The symptoms having been greatly relieved by the first series in which 3 Gm. was given, a second series containing about the same amount was employed. About six weeks later the syndrome of a lipoid nephrosis appeared and ended fatally.

Bone Graft to Increase Diameter of Contracted Pelvis

In the Paris letter, June 6, reference was made to a paper by Delagénière of Le Mans reporting eight cases of contracted pelvis, which were enlarged by bone grafts taken from the patients' tibias. In his paper read at the March 17 meeting of the Académie de chirurgie, Delagénière reported a case in which a normal delivery had followed sixteen months after the bone graft operation. At the July 8 meeting of the same society, Delagénière reported a second case in which he had enlarged the anteroposterior diameter of a contracted pelvis by a bone graft in June 1934 and a normal delivery had taken place in May 1936. Roentgenograms of seven of the nine cases were shown at the July 8 meeting. In three cases, dating back two years eight months, two years ten months and four years, the graft is still visible between the ends of the pubic bones.

The history of the case reported at the July 8 meeting was as follows: A primipara, aged 22, entered the clinic June 1, 1934. Several attempts to deliver the presenting head at the inlet by forceps being unsuccessful, a symphysiotomy was done, followed by delivery of a normal child weighing 5,000 Gm. Twelve days later, two grafts 6 cm. long were taken from the patient's left tibia and placed between the separated pubic bones. The patient reentered the clinic to be confined again. Radiography revealed that the separation between the pubic bones had been well maintained since the operation in June 1934. The fetus was as large as the first one, but delivery occurred spontaneously in five hours without incident.

BERLIN

(From Our Regular Correspondent)

Sept. 28, 1936.

Close Roentgen Irradiation as Substitute for Radium Therapy

In the treatment of cancer, radium therapy has heretofore been regarded as superior to roentgen irradiation. This superiority has been particularly well demonstrated in cancers of the skin, lips, oral cavity and female genitalia. In such cases the results of roentgenotherapy were unimpressive, virtually nil. Hence centers for anticancer activities came to be established at which deposits of radium could be procured. But the supply has still been insufficient, owing to the high cost of radioactive substances. Professor Chaoul of the Sauerbruch clinic, Berlin, discussing this topic in the Berlin Medical Society, furnished the following statistics on the varying radium supply in different countries, computed for each million of population: Sweden, 1.8 Gm. of radium; Great Britain, 1.7 Gm.; Denmark, 1.8 Gm.; Czechoslovakia, 1.6 Gm.; France, 1.2 Gm.; United States, 1 Gm.; Germany, 0.3 Gm. The Swedish radiologist Forsell places the national radium supply necessary for the proper treatment of cancer at 2.5 Gm. per million of population. As the foregoing figures show, no such requisite amount has been available in any country and least of all in Germany.

In view of this situation, Chaoul undertook to experiment with so-called close roentgen irradiation and found that the hitherto assumed superiority of radium lay not in the quality of the rays but merely in the physical-technical circumstances of their application. He then attempted a carefully supervised adaptation of the circumstances of radium therapy to the administration of roentgen rays. Especially important in both therapeutic procedures was the pronounced diversity of the geometric distribution of the dosage in the tissue. In radium therapy the loss of energy in the tissue takes place quickly according to the depth and the lateral aspect. Extremely

powerful doses can therefore be delivered at the focus without any serious damage to the surrounding tissues. This is shown biologically by the preservation of the parent tissue and of the defense mechanisms necessary for the curative process. (In high voltage therapy, on the other hand, the objective is a thorough homogeneous irradiation of tissue layers and the healthy may be injured in the process.) Roentgen irradiation had therefore, like radium therapy, to be based on a decrease in dosage. It was possible to effect this adaptation by considerable shortening of the focus-skin distance, by application of proportionately soft rays and by the greatest possible restriction of the field of irradiation to the diseased area. In addition, the adaptation of both the time element and the duration of the effects of irradiation are taken into account. The biologic importance of prolonged radioactivity has in recent years been determined for radium by Régaud. In close roentgen irradiation, scattered doses were accordingly administered over a period of from three to four weeks. The assimilation of the maximal dosage too is successful; in radium therapy doses of some 8,000 roentgens are regarded as destructive of cancer and applied accordingly. In close roentgen irradiation by the restricting of the irradiated area and the scattering and extension of the dosage over several days, dosage of from 8,000 to 10,000 roentgens could be, according to Chaoul's reports, smoothly administered without any irreparable damage.

Thus, if all these requirements are satisfied, roentgen irradiation may be largely substituted for radium therapy. During the past four and one-half years 281 cancer patients were administered the roentgen treatment, the sphere of indication being the same; namely, directly accessible tumors. Chaoul outlined the successful results obtained by him: skin carcinoma cases, 93 per cent cured; cancers of the lip, 83 per cent cured; cancer in the oral cavity, 40 per cent, results in no way inferior to those obtained by radium therapy. Chaoul has also observed notable cures in cases of melanoma.

Encouraged by the foregoing satisfactory use of close roentgen irradiation in directly accessible cancer of all kinds, Chaoul is now attempting to apply the same procedure to cancer of the internal organs and thus to render surgical intervention unnecessary. Close irradiation is particularly suitable in rectal carcinoma because of the easy operative accessibility. The procedure is as follows: The coccyx and the under part of the sacrum were resected after the establishment of a preternatural anus, the rectum was drawn down posteriorly and dissected in its longitudinal aspect at the level of the tumor, and its walls were attached to the skin wound with several sutures. Irradiation succeeds then just as in superficially situated cancers; it is continued till complete atrophy of the tumor has taken place (a check should be made by repeated biopsies); then resection and so on takes place. To date this treatment has been given in only nine cases of rectal carcinoma. In seven the tumor completely disappeared, the first case has meanwhile been under observation for two and one-fourth years and the second for one and three-fourths years without any recurrence being noted. These cases are especially noteworthy if one recalls that the average expectation of life in cases of inoperable carcinoma of the rectum is one year. These results also serve to disprove the idea that carcinomas of the rectum are refractive to the rays.

Chaoul's next task will be so to improve the technic that it may be applied to those deep seated tumors for which a combined surgical and roentgen therapy is indispensable.

The Value of Determination of Blood Type

The National Health Council functioned as an expert advisory adjunct of the National Bureau of Health till 1933. In this capacity it instituted a subcommittee to investigate the forensic value of blood type determination and in 1929 this committee issued the following statement: "According to medicolegal expert opinion, blood type determination when skilfully conducted is a reliable forensic aid, particularly in cases involving study of blood stains and the determination of paternity. In many such cases a decision may be arrived at by determination of the blood type when all other evidence is inadequate. Without this procedure the establishment of the facts of a case and the exculpation of a person unjustly accused of wrong-doing would in many instances be impossible." The German courts have subsequently adjudicated all cases concerning support of children and disputed legitimacy of children in accordance with this expert opinion.

But recently the minister of justice has communicated the opinion of a medicolegal expert which casts doubt on the reliability of blood type determination. This opinion sets forth that many aspects of the question call for a certain caution. As long as so much about blood typing remains obscure, a blood type finding cannot be regarded as conclusive evidence but only as indicative of probability. The minister forthwith made public a new authoritative pronouncement on the foregoing opinion by the National Bureau of Health, the contents of which are substantially as follow: The medicolegal expert is of the opinion that the determination of a blood type serves as a valuable index of probability but is inadequate as a sole means of proof in criminal procedures. This view differs from that of serologists and forensic physicians who are actually working in the field of blood typing research. Whenever he refers to so-called variant cases he has in mind that which he has long considered old and unreliable raw material. Tests of the heredity of families the members of which are completely in sympathy with the purpose of the examination and desire such examination reveal no variation (cases of illegitimacy are virtually automatically excluded from this group). In cases that present alteration of the blood group type or deviations from the generally accepted laws of heredity it has been frequently demonstrated that either the test is faulty or the children are illegitimate. Throughout innumerable legal cases the determination of blood group quality A and B and of the blood corpuscle characteristics M and N are frequently mentioned as the sole means of proof. There is no occasion, therefore, for qualification of the foregoing opinion of the National Bureau of Health. It is presumed, to be sure, that the examination will be undertaken on the basis of complete factual data.

Substitutes for Gold in Dental Fillings

It is reported from a convention of "dentisten" (the dental practitioners who lack regular training), held at Frankfort-on-the-Main, that an important economic question confronts the group; namely, how the relatively large amount of gold that heretofore has been utilized in the manufacture of artificial teeth and which even today appears to be in part indispensable can be replaced by some other material. Normally, that is, in times when the gold supply did not figure so largely as it does today, the German dental physicians (zahnaerzte) and the dentisten required an annual average amount of 5,000 Kg. of gold in the course of their practice of dentistry. It has been possible to decrease this required amount by some 45 per cent and the effort is now being made to effect even further reductions. In their search for a substitute material, in view of the diminishing gold supply, the dental practitioners have turned to platinum-base alloys. At the convention, discussions were submitted on silver-palladium alloys and other new metals, some of which contain gold in varied amounts. The tendency to utilize these and other white metal alloys for crowns, cast fillings and prosthetic pieces has been evident for the last two years and should partially solve the problem of a satisfactory substitut for gold. Those who advocate white metal alloy as a dental replacement material—and that means the entire group of dentisten—doggedly insist that the new metal should by no means be considered a "gold substitute" but as a new working

medium the manufacture and use of which renders gold unnecessary for many procedures of dentistry and in this way, they say, the amount of gold saved can be utilized for more urgent economic ends.

ITALY

(From Our Regular Correspondent)

Sept. 30, 1936.

Hemorrhagic Allergy

Prof. Giuseppe Sanarelli of Rome University, also a senator, in a lecture delivered to the physicians of the army spoke on hemorrhagic allergy, also called Sanarelli-Schwartzman's phenomenon. The speaker reviewed the difficulties in the attempts to reproduce experimentally typhoid, cholera, dysentery and intestinal anthrax. These diseases are intestinal reactions to a general infection (which is due to the entrance of specific bacteria into the blood through Waldeyer's pharyngeal lymphatic ring) rather than intestinal local infections. The phenomenon of hemorrhagic allergy was observed by the speaker, for the first time, during his studies on experimental cholera, during which he isolated accidental bacteria, especially colon bacilli, from the blood of cholerous guinea-pigs. With a picture similar to that of acute cholera in human beings, death takes place in guinea-pigs which are first injected with a sublethal dose of cholera vibrio and second with a small harmless dose of a culture of colon bacilli. At necropsy epithalaxia of the intestinal mucosa (Sanarelli's phenomenon) is found in all cases. The speaker thinks that acute appendicitis is caused by a phenomenon equal to cholera epithalaxia. Owing to a condition of either chronic or subacute inflammation, the appendix acquires a condition of sensitization to the bacteria. If the latter, for some reason, enters the blood, acute appendicitis develops. The speaker succeeded in reproducing experimental acute appendicitis in rabbits by this pathogenic mechanism. He includes acute appendicitis within the chapter of hemorrhagic allergy. Schwartzman observed that Sanarelli's immunitary reaction takes place also in the skin (Schwartzman's phenomenon). More recently the reaction has been reproduced almost in all organs, with the exception of the liver, the central nervous system and the adrenals. Hemorrhagic allergy differs from anaphylaxis. Anaphylactic sensitization takes a long time to be produced and the reaction is induced by inoculation of specific bacteria, identical to the antigen that was used in sensitizing the organism. Allergic sensitization is produced in a few hours and the reaction takes place by injection of filtrates of different bacteria than the one used in producing sensitization. The speaker stated that the sudden acute crises of several diseases, such as colic pain, pneumonia and hemorrhagic pancreatitis, can be interpreted as phenomena analogous to those seen in experimental hemorrhagic allergy.

Castellani Lectures on Italian-Ethiopian War

Prof. Aldo Castellani, head of the Clinic of Tropical Diseases at Rome University, a senator and general adviser on sanitation in eastern Africa, in a lecture recently delivered to the Istituto della Sanità Pubblica, spoke on health and sanitation of the Italian army during the Ethiopian war. There were 500,000 Italian soldiers and 100,000 Italian workers. The army mobilized 135 camp and base hospitals (with a bacteriologic laboratory and a roentgen equipment for each base hospital), fifty-five ambulatory brigades of sanitation, thirteen surgical units, fifteen ambulances for roentgen work, eleven odonto-iatric ambulances, four central laboratories, twelve brigades for disinfection, six brigades for sanitation of the soil, 139 equipments for making water potable and an abundant supply of sanitary material. The army had twenty hospitals and infirmaries along the coast and eight hospital ships, six of which had conditioned air and refrigeration centers. There were also thirty colonist hospitals. The sanitary personnel comprised about 2,500 physicians (the majority of whom had taken courses at the Clinic of Tropical Diseases at Rome), 385 nurses of the Red Cross, 200 religious sisters and about 16,000 sanitarians and assistant workers. Diseases, especially tropical, among Italians were as follows: 1,241 cases with twenty-three fatalities from pernicious malaria, 453 hospital cases of dysentery (with a predominance of amebic dysentery) with one fatality, seventeen cases of recurrent fever with no fatalities, five cases of dengue with no fatalities and one case of smallpox, which ended in recovery. No cases of exanthematic typhus, scurvy, smallpox, leprosy, plague or cholera developed among the Italians. All soldiers were given lemon juice every other day (one lemon each). Prevention against malarial larvae could not be made. Soldiers in all ranks were daily given three tablets of quinine. In the Italian colonies of Somaliland and Eritrea, 458 cases of typhoid-paratyphoid with 161 fatalities were reported. From experience in colonial wars in the past it was expected to have a larger number, of about 50,000 Italians, taken ill and also to have a death rate of several thousand from diseases. The satisfactory services of sanitation and the hygienic and other measures taken and the administration of vaccines, especially polybacterial vaccines, resulted in the satisfactory health conditions of the troops all through the war. There were thirty cases of sunstroke, with seven deaths. The small number of cases of sunstroke, regardless of the fact that the activities took place in the torrid zone, were due to precautions taken with the troops. Drinking of alcohol was prohibited, except by the daily allowance of wine given to the soldiers at evening. All soldiers wore comfortable helmets, and transportation whenever possible was made by motor. There were many cases of dengue among civilians at Massaua when the Italian troops landed. To prevent contagion by mosquito bites the camps were placed on the highlands. Mortality of soldiers in eastern Africa was lower than that of the metropolitan army.

Deaths

Prof. Ottorino Rossi, head of the Pavia University, director of the clinic of mental and nervous diseases in Pavia and author of several books on neuropsychiatrics, is dead.

Prof. Arcangelo Ilvento, vice director of public health, is dead. During his life he had important positions in the Italian Red Cross and the social association of public welfare. Recently he was appointed inspector of sanitation. He was a collaborator in sanitation of eastern Africa and an active worker in the prevention and crusade against malaria and trachoma. He made the basis and laws of the insurance societies against tuberculosis. He wrote several books on bacteriology, epidemiology, sanitation, social medicine, hygiene for children in schools, social aspects of tuberculosis and history of knowledge on malaria. Several of his books have been translated into other languages.

Marriages

JAMES CLIFFORD SCOTT JR. to Miss Mary Helena Devereux, both of West Chester, Pa., September 11.

VINCENT O. LESH, South Amboy, N. J., to Dr. RUTH J. ELLIS of Fayetteville, Ark., September 4.

LLEWELLYN HALL to Mrs. Caroline Doane Fogg, both of West Hartford, Conn., September 11.

THOMAS GEORGE KNOWLTON to Miss Grace E. Kent, both of Toronto, Ont., Canada, August 22.

RICHARD STERLING HERRING, Richmond, Va., to Miss Marie Hurd of Chicago, September 2.

ARTHUR T. LEGG, Boston, to Miss Marie L. Robinson of Brookline, Mass., August 27.

JESSE POLK LOCKHART to Miss Margaret Caldwell, both of Pharr, Texas, September 10.

ALBERT G. SCHUTTE, Milwaukee, to Miss Ada Bernice Hopkins, July 18.

Deaths

Isaac Max Rubinow, Cincinnati; University of the City of New York Medical Department, 1898; executive secretary of the social insurance committee of the American Medical Association, 1916-1917; examiner for the U. S. Civil Service Commission, 1903-1904; economic expert for the Bureau of Statistics, U. S. Department of Agriculture, 1904-1907; member of the Bureau of Statistics, U. S. Department of Commerce and Labor, 1907-1908; member of the Bureau of Labor, 1908-1911; chief statistician for the Ocean Accident and Guarantee Corporation, 1911-1916; in 1917 director of the Bureau of Social Statistics, Department of Public Charities, New York; past president of the Pennsylvania State Conference on Social Work; formerly director of the Zionist Organization of America; directed the establishment of several hospitals in Palestine, 1919-1923; for several years director of the Jewish Welfare Society of Philadelphia; had been engaged in social and editorial work; aged 61; died, September 1, in the Montefiore Hospital, New York.

Henry Farnum Stoll ⊕ Hartford, Conn.; Columbia University College of Physicians and Surgeons, New York, 1902; past president of the Hartford County Medical Society; governor and fellow of the American College of Physicians; served during the World War; on the staffs of Wildwood Sanatorium, Hartford, Windham Community Hospital, Willimantic, Manchester (Conn.) Memorial Hospital, New Britain (Conn.) General Hospital and the Bristol (Conn.) Hospital; aged 58; died, September 28, of coronary thrombosis.

Cyrus O. Jaster, Elyria, Ohio; Western Reserve University Medical Department, Cleveland, 1898; member of the Ohio State Medical Association; past president and for many years secretary of the Lorain County Medical Society; at various times on the staffs of the Elyria Memorial Hospital, Cleveland State Hospital and St. Alexis Hospital, Cleveland; aged 59; died, September 6, in St. Vincent Charity Hospital, Cleveland, of coronary sclerosis and pulmonary infarction.

Philip C. W. Johannes, Chicago; Northwestern University Medical School, Chicago, 1900; clinical assistant in genitourinary surgery at his alma mater, 1904-1906; member of the Illinois State Medical Society; served during the World War; member of the staffs of the Illinois Masonic Hospital and the Evangelical Hospital of Chicago; aged 60; died, September 8, in St. Margaret's Hospital, Hammond, of injuries received in an automobile collision.

Helen Correll-Loewenstein, New York; Woman's Medical College of the New York Infirmary for Women and Children, New York, 1898; for many years on the staff of the New York Orthopedic Dispensary and Hospital; aged 72; died, September 7, at her summer home in Bernardsville, N. J., of arteriosclerosis, diabetes mellitus and cerebral hemorrhage.

Robert Stirton Thornton, Vancouver, B. C., Canada; University of Edinburgh Faculty of Medicine, Scotland, 1884; formerly chairman of the school board of Deloraine, Manit., and member of the legislature of Manitoba; at one time minister of education and president of the Medical Council of Canada; aged 73; died, September 18, of coronary thrombosis.

Benjamin Augustus Littell, Opelousas, La.; Tulane University of Louisiana Medical Department, New Orleans, 1888; formerly secretary of St. Landry Parish Medical Society; at various times mayor, parish coroner and health officer of Opelousas; past president of the city and the parish boards of health; aged 70; died, September 4.

Gordon Lee Hastings ⊕ Little Rock, Ark.; Medical College of Virginia, Richmond, 1926; fellow of the American College of Physicians; assistant state health officer and director of rural sanitation, state department of health; formerly health officer of Union County; aged 38; died suddenly, September 14, in Emporia, Va., of heart disease.

John Davidson Hunter, Rayne, La.; Memphis (Tenn.) Hospital Medical College, 1902; member of the Louisiana State Medical Society; formerly member of the state legislature and mayor; parish health officer; aged 60; died, September 16, in the Touro Infirmary, New Orleans, of cerebral hemorrhage.

Guy Howard Swan ⊕ Beachwood, N. J.; Michigan College of Medicine and Surgery, Detroit, 1903; member of the Radiological Society of North America; served during the World War; member of the staff of the Paul Kimball Hospital, Lakewood; aged 55; died, September 8, of coronary occlusion.

Franklin Trumbull Wilcox ⊕ La Porte, Ind.; Rush Medical College, Chicago, 1890; formerly secretary of the county board of health and member of the city board of health; past president of the La Porte County Tuberculosis Association; aged 70; died, September 13, of coronary occlusion.

De Witt Kluttz, Washington, N. C.; University of Pennsylvania Department of Medicine, Philadelphia, 1918; member of the Medical Society of the State of North Carolina; for many years a member of the staff of the Tayloe Hospital; aged 47; died, September 8, of coronary thrombosis.

Charles Stanley Grahame Jr., Summitville, Ind.; Indiana University School of Medicine, Indianapolis, 1933; aged 29; died, September 23, in a hospital at Hazard, Ky., of injuries received when a motorcycle on which he was riding collided with an automobile.

John Alton Gillen ⊕ Rice Lake, Wis.; University of Minnesota Medical School, Minneapolis, 1934; on the staff of the Lakeside Methodist Hospital; aged 32; died, September 1, in St. Francis Hospital, Evanston, of cirrhosis of the liver and cerebral edema.

Clarence Light Carlton ⊕ Moline, Ill.; Northwestern University Medical School, Chicago, 1903; served during the World War; on the staffs of the Lutheran Hospital and the Moline Public Hospital; aged 65; died, September 9, of carcinoma of the colon.

Samuel Thomas Tapscott, Searcy, Ark.; University Medical College of Kansas City, Mo., 1907; member of the Arkansas Medical Society; served during the World War; aged 51; was found dead in his office, September 4, of a self-inflicted bullet wound.

Albert Smith, Parsons, Kan.; Chicago Homeopathic Medical College, 1895; member of the Kansas Medical Society; for many years a druggist; formerly on the staff of the Mercy Hospital; aged 66; died, September 13, of chronic nephritis.

James Archibald Edwards ⊕ Oakdale, Iowa; University of Nebraska College of Medicine, Omaha, 1904; superintendent of the Iowa State Sanatorium; aged 61; died, October 5, as the result of injuries received in an automobile accident.

John Herbert McConnell, Toronto, Ont., Canada; Trinity Medical College, Toronto, 1897; fellow of the American College of Surgeons; surgeon to the Grace Hospital; aged 60; died, September 15, of coronary thrombosis.

Frederick Erastus Hyde, New York; Bellevue Hospital Medical College, New York, 1874; member of the Medical Society of the State of New York; Civil War veteran; aged 92; died, September 16, of chronic nephritis.

James Edgar Murray ⊕ Piqua, Ohio; Atlanta (Ga.) Medical College, 1893; past president of the Miami County Medical Society; on the staff of the Memorial Hospital; aged 78; died, September 5, of cerebral hemorrhage.

Hester Brewer Smith, Dallas, Texas; University of Texas School of Medicine, Galveston, 1915; served during the World War; aged 46; was found dead, September 1, of a self-inflicted bullet wound.

Archibald Adams Reid, Oneonta, N. Y.; Long Island College Hospital, Brooklyn, 1883; aged 77; died, September 13, in a hospital at Utica, of diabetes mellitus and bronchopneumonia.

Harold McClellan Allen, Toronto, Ont., Canada; McGill University Faculty of Medicine, Montreal, Que., 1922; L.R.C.P., London, and M.R.C.S., England, 1924; aged 40; died, August 3.

Edward Benjamin Taylor, Milwaukee; Hahnemann Medical College and Hospital, Chicago, 1897; aged 62; died, September 1, in Rochester, Wis., of coronary sclerosis and angina pectoris.

De Ruyter Howland ⊕ Stratford, Conn.; Columbia University College of Physicians and Surgeons, New York, 1906; health officer of Stratford; aged 54; died, September 12.

William Gray Swank, Crawfordsville, Ind.; Beaumont Hospital Medical College, St. Louis, 1892; formerly city health officer; aged 76; died, September 4, of heart disease.

David Montefiore Foss, Gouverneur, N. Y.; University of Vermont College of Medicine, Burlington, 1886; aged 76; died, September 8, of myocarditis.

Martin Andrew O'Neill, Baltimore; University of Maryland School of Medicine, Baltimore, 1900; aged 61; died, September 9, of chronic nephritis.

Edward E. Whitehorne, Vesper, Wis.; Albany (N. Y.) Medical College, 1878; aged 80; died, September 16, of arteriosclerosis.

Correspondence

WATER, WATER, EVERYWHERE

To the Editor:—A few years ago I appealed to you as the fountainhead of information to know whether or not to give all my patients lots of physics. You did not reply but published my letter and I promptly received many replies from all over the country. Again my head is in a whirl. I find I am living in the center of the therapeutic Sahara Desert of the world. All our patients are dehydrated, desiccated and destined to destruction. They are drying up. Water, water everywhere and every one short on water. It's a sad predicament. I find it a bit difficult to determine just how nearly my patients are about to blow away, but this difficulty does not seem to be shared by many others. A hospital patient who has not had an intravenous injection of fluid the first three hours after getting well settled down between his rubber sheets has probably just neglected to engage a physician. A hospital record that does not include forced water is always laid aside for special discussion, inquiry and, probably, criticism. There is now a movement on to make it routine to hydrate all patients and then make the diagnosis, just as a friend of mine does who immediately injects solution of posterior pituitary and then determines whether or not the woman is in labor. Once in about five it saves time. As the aquatic squad approaches a ward, the patients yell "Here come the Marines."

These hydration specialists have lots of backing. You can't read anything in medicine or the lay press without being informed that you should "push water." It's about the only remedy medicine offers that all the cultists have whole-heartedly accepted; so there must be a lot to it. Every time a country newspaper adds a new medical columnist, the town waterworks has to drill extra wells. Every time the schools adopt a new and up-to-date physiology they have to add one or two fountains and some other plumbing. Some schools tried "water drinking drills" like fire drills but had to give them up because of shortage in facilities, and now we do not know and may never know whether it is safe to allow school children to face the future without these drinking drills. From my own children I learned that each child should become water conscious and react to the sight of a fountain very much as a dog does to a tree, except in reverse. They should start the day with two big glasses before breakfast and then a milk cereal. These wash out all the poisons and toxins that congregate in a child's body through the night. It seems that the child can work off the poisons that develop through the day fairly well, but the night poisons, they are something different. It takes lots of water. My younger child is a perfect convert and a great believer in school textbooks. She thought once she could hear the water chasing the poisons round about in her innerds and begged me to listen, but all I heard was bubbles. When I did not enthuse over her water program she suggested that I might be behind times, as all of her teachers had advised them many times always to drink all the water they can hold.

Every one knows that in case of a cold one should fairly swim in water. Since no one ever heard a fish sneeze, how can it be otherwise? Drinking lots of water for colds (with soda, apples or limes) always did look logical to me, for when your eyes, nose and lungs are spouting out pints of liquids it shows you are short on water or something. Besides, it seems reasonable to assume that if the water pouring out of these openings doesn't wash out the cold where it is, more water will start spoutings elsewhere and wash it out where it isn't. Plenty of water in at the top and lots of physic from the bottom will often flush out a cold before it decides where to locate, fairly catching it in midair and totally off its guard. I'll admit that I have worried a bit about the effect to gravity on a very wet cold as compared to a dry one, and it hasn't always been clear to me how soaking up a cold till it drips will prevent it from extending itself rather aimlessly about *ad lib* and *cum laude*.

Empirically but with a fanfare of superscience, all diseases are rapidly realining themselves into two great groups, the washable and the unwashable. In the early days of this movement only a few were in the first group and it was easier to name them and regard the unnamed as belonging to the unwashable class; but we have made so much Progress that now it is far easier to name the latter and regard all others as candidates for the great flood. The definitely unwashable consist of alopecia, freckles, atheroma callus, chloasma, blackheads, dyshidrosis, dandruff and housemaid's knee. There are others but not many and you will note that they are surface diseases, just where you might think a good washing would help. Now to be fair I must add that the very wildest irrigating enthusiasts do not maintain that their universal placebo will be harmful in these cases. They merely feel that it is not definitely indicated, and after you have talked with one of them for a few minutes you will concede that that is some concession.

A friend related to me that one of the most comical sights he ever witnessed was once when he was driving through the hills of Connecticut and came to a filling station. While the regular attendant was filling his car, the attendant for the Colon Flushing Department with full equipment was chasing a half disrobed and screaming woman among the outhouses and through the garden. Even after he had sold her on the idea, she still didn't know that that was where her colon was located. Such experiences practically killed the lay monopoly of this life-saving procedure and returned it to our brother disciples where it belongs, if it belongs.

Now we wash out and away the last vestige of most diseases at every natural opening of the body and if there are difficulties we punch new openings. We wash out pyelitis, even when it consists largely of cortical abscesses, and baptize nephritis regardless of conditions with the same assurance with which a colored preacher douses his converts. We add quarts of water to the diet of a patient with cystitis though it dilutes his medicine and causes extra painful voidings, to wash out what? If we know no physiology there is no thought more logical than the idea that drinking excessive amounts of water will prevent constipation. We saturate a tuberculous patient who seems disposed to dry up on our hands, for what reason? Specialists in tuberculosis claim that a dry lung is a therapeutic ideal. We force water on squishy babies whether they are dehydrated or not, and for what reason? Not that some of them do not need it but do they all, especially the squishy kind? We ask dried-up old people to increase their water intake, and who ever heard of an old person in health drinking much water? That may be one reason why they are old. We pump in large quantities, or at least we used to, in cases of threatened or actual eclampsia to wash out the "toxins" that no one can find and now learn that too much water is the cause. A patient has a traumatic head. There is not much we can do about it, so why not fill his skin and cavities with lots of water and increase his intracranial pressure? In case of doubt, give big intravenous injections. Next to blood transfusions they create the most certain impression the physician knows what to do and does it *pronto*. Never fail to take the relatives into consideration. We get a case of fits, just any kind or age, and decide instantly that everything is going out and nothing coming in, so we decide that something should go in in a big way—water—sometimes with salt, other times with sugar and other times with both and let them fight it out and let the best chemical win. Since Hippocrates we have known that during convulsions the brains are "wet" but maybe it was the wrong kind of moisture. Something has to be done. Last week a street car conductor complained that his work required that he stay with his car and

that he did not get to drink enough for his health. I suggested a job as attendant at Boulder Dam. We prepared our prostatics who have been damming up water in every niche of the body for months by putting them to bed, draining and forcing water for two to six weeks—that is, those do who do it that way. Maybe some have changed. Reversed hydrostatics have about ruined their renal apparatus, so these patients are asked to give nature's method, physiologic rest, reversed action and enforced maximum activity. They claim that the draining releases some of the toxins but that the washing really does the big trick. Seems as sensible as vinegar for sore eyes, but custom and usage demand the procedure. One surgeon is said to have claimed that he didn't regard his patient as adequately prepared if a spray of water did not issue from his incision.

Even I admit that there are many instances when replacing lost or strayed fluids is highly indicated, but I have about arrived at the conclusion that there are a few other instances where the procedure is "the bunk" and I have definitely decided that thirst is a fair guide for water needs for one whose mind is clear and whose gullet is open.

E. O. HARROLD, M.D., Marion, Ind.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

KETOGENIC DIET IN PETIT MAL

To the Editor:—I wish to ask some advice of you. I have a daughter who is 18 years old. There were no birth injuries and no other trouble except mild ileocolitis the first year. She had lobar pneumonia at 2 years, possibly with encephalitis complicating. Appendectomy was performed at 5 years. At the time of this operation her mother noticed that she turned her eyes upward and thought it just a habit. The mother told me about the eye trouble and I at once felt that she was having petit mal. This condition grew worse, until at 7 years of age she was having the spells of turning the eyes upward every two or three minutes, the attack lasting a few seconds each time. I was advised that it probably was a brain tumor. A neurologic surgeon attempted to inject air into the ventricles with no success but caused a spastic paralysis on the left side. I later put her on the ketogenic diet. That practically controlled the attacks, but she had a nutritional edema, and I discontinued the diet. I have had her seen by at least six different neurologists and neurologic surgeons, and nothing seems to be of any benefit. Also she has been through the mill of the allergist without results. At the present time these spells are harder than in the beginning, the eyes turning up and the upper part of the body nodding a little. If she is carrying a dish with something in it, she may spill something out of it but not drop the dish. At times the spells are long enough so that she may lose connection in the conversation. Early in the morning at times she may have one every three or four minutes, but as the day passes it may be half an hour between spells. When she is at her best she may not have more than one every half hour early in the morning and less frequently as the day goes on. She has had at least one general convulsion. After all these efforts it must apparently be admitted that the condition is epilepsy, possibly caused by an encephalitis at the time of the pneumonia. She did average work in school except in mathematics, in which she did poorly. She was graduated from high school last spring. In subjects like history and English she often made A and B. She is a lovable child except for being at times somewhat moody and obstinate, but on the whole she is very likable. She is beginning to see that she has a hard time maintaining her place with people and is beginning to get resentful and to seclude herself somewhat. She has an unusual amount of energy and is resentful for not being able to do more and better than any one else. She can be sent to college, but what kind, and where is there something that she can do so that she can be protected and do something of benefit to her? I should like to be advised and if you can refer me to some one capable of taking up the subject and helping me I shall appreciate it. Of course, keep in mind, in considering the case, her locality and not advise me to consider something too far away. Please omit name.

M.D., Kentucky.

ANSWER.—The opinion expressed regarding the nature of the attacks and the underlying cause is probably correct. There is a possibility that the attacks may yield to the administration of stramonium. The powdered leaf may be given as a test in a dose of 0.12 or 0.2 Gm. three times daily, over a period of three or four days. If improvement is not apparent by that time, some other form of treatment should be tried. Such attacks often do not yield to phenobarbital and another trial with the ketogenic diet is worth considering. When this diet was introduced, nutritional disorders were encountered. To prevent these, yeast should be added to the diet and 1 Gm. of calcium phosphate given each night. Needless to say, the urine should be tested daily to make certain that a state of ketosis actually exists.

It is well to encourage the kind of work that leads to a normal physical, mental and social development of the patient. The patient's own wishes as to the kind of work selected should, of course, be considered, which makes it difficult to give more specific advice.

NEPHRALGIA

To the Editor:—A white woman, aged 36, has a severe bilateral nephralgia extending over a period of the past six years. At the time she came under my care in June 1935, she had been getting one-half grain (0.03 Gm.) of morphine daily for three or four months. Intravenous and retrograde pyelograms show definite bilateral kinking, but no obstruction at all as evidenced by the fact that there is no dilatation at all above the kink. She is now getting the same relief from one-eighth grain (0.008 Gm.) of morphine as she formerly had from one-half grain. There is no pus or albumin in the urine, and phenolsulfonphthalein is eliminated about 80 per cent in two hours (intramuscular). General nutrition is excellent. In October she was operated on, the left kidney being freed from fat and delivered from the wound; the muscle was sutured together beneath the kidney, which was left immediately subcutaneous. Partial relief has followed on this side. Thinking that the pain might be in the nature of a neuralgia and that temporary interruption of the pain pathway might result in relief, I injected 75 mg. of procaine hydrochloride intraspinally. She had complete relief for seventy-two hours and seemed to be in Heaven, but then her pain returned as before. I am wondering whether there is any way in which the pain pathways can be interrupted, by section or injection, or if you have any other suggestions to offer. Please omit name.

M.D., Michigan.

ANSWER.—For a woman, aged 36, suffering with bilateral nephralgia, a limited experience apparently justifies a sympathectomy of the renal vessels and ureter on both sides. Mr. S. Harry Harris of Lewisham, Sydney, Australia, appears to be quite enthusiastic about such a procedure. It is possible that a subdiaphragmatic splanchnic nerve section with removal of the upper two lumbar ganglions may be more effective than the renal sympathectomy, since the latter operative procedure would include a sympathetic denervation of the entire urinary system rather than being limited to the kidney itself.

It would be unwise to attempt any radical procedure without the preliminary study of a nerve block. Successful splanchnic nerve blocks should be employed as therapeutic tests previous to any type of sympathectomy.

The continued use of morphine naturally arouses the suspicion of morphine addiction, for if there is an addiction the pain may not be of organic character, and therefore all operative procedures would fail.

TOXIC ERYTHEMA

To the Editor:—I have a case of erythema multiforme that is very resistant to treatment and I should like you to make some suggestions as to treatment.

W. G. ELLIOTT, M.D., Cuthbert, Ga.

ANSWER.—Erythema multiforme belongs to the group of toxic erythemas. Some authorities include many of them under the title erythema multiforme. Others insist that only those of unknown etiology presenting the typical acute lesions on the hands and feet and mucous membranes are admissible as erythema multiforme. From the statement in the query that the case is resistant to treatment, a doubt is raised at once that the case is one of the typical ones, for they usually subside spontaneously in a few weeks. There are several rare dermatoses to be considered under the heading of chronic erythema multiforme, but without a description of the case in question no intelligent surmise of its place in this group can be made. See Ormsby, Diseases of the Skin, Philadelphia, Lea & Febiger, 1934, pages 137 and 138. Granuloma annulare and erythema elevatum diutinum might also be considered.

If the case belongs to the group of toxic erythemas, every effort should be made to determine its etiology. The first possibility to be investigated is that some drug is responsible. Phenolphthalein, arsphenamine, antipyrine, inorganic arsenic, mercury, potassium iodide or antistreptococcic serum may be suspected. Foods, as fish, shellfish or cheese, are sometimes responsible. The relation of erythema multiforme to purpuras would accentuate this possibility. Infections, especially streptococcic infections in the teeth or the tonsils, the puerperal

uterus, malaria, gonorrhea and many other diseases not to be considered in relation to the present case are able to cause a toxic dermatitis. Syphilis rarely causes such an eruption. Bloch reported two cases of an erythema multiforme-like eruption in cases of ringworm in which trichophytin injections had been given. Tachau (Handbuch der Haut- und Geschlechtskrankheiten **6**:616) does not admit such toxic erythemas as erythema multiforme. He limits the term to typical acute cases presenting concentrically evoluting eruptions on the hands and feet, and bullous eruption of the oral mucosa, self limited but recurring from time to time. He believes that these are due to some specific cause, probably an infection yet undiscovered.

For treatment of such cases, salicylates take the first place; calcium salts are helpful. Tachau quotes W. S. Lain (X-Rays in Erythema Multiforme, THE JOURNAL, May 1, 1909, p. 1405), who used small doses of x-rays on two days in succession, and another on the fifth day of treatment, after which the lesions subsided. A recurrence thirteen days later was given similar dosage on three successive days and again subsided. The backs of the hands are quite susceptible to x-rays and six doses within three weeks would necessarily be small, probably about one-eighth skin unit (37 roentgens). This is worth trying, if investigation does not alter the diagnosis.

NARCOLEPSY

To the Editor:—Will you advise me concerning the possible causes of persistent recurring sleepiness occurring in a man of 55, a lawyer, in excellent physical condition except for a chronic sinusitis of thirty years' duration, which is probably due to an allergic sensitivity if one may judge from the large number of eosinophils in the nasal secretion and 8 per cent in the blood stream. No other organic ailments are demonstrable. The sleepiness comes on when he reaches the office in the morning or shortly after and is relieved by getting up and walking outside but again recurs. Outdoor exercise, such as golfing, relieves for several hours. He sleeps well at night and feels refreshed in the morning. This has been of some five years' duration but is gradually getting worse and interferes seriously with his work, especially when in court. I will appreciate greatly any help you can give me. If this is published, please omit name and address.

M.D., Oregon.

ANSWER.—The patient is most probably suffering from narcolepsy, as the attacks of somnolence appear to be truly pathologic. The inquirer does not state whether he has any attacks of weakness when he has any emotional upset, such as becoming angry, or from surprise, which occasionally occur in persons with such attacks of somnolence. He may be placed on ephedrine sulfate, 0.024 Gm. (three-eighths grain), two or three times a day, as this preparation should relieve him materially. Benzedrine sulfate has also been recommended for the treatment of narcolepsy. This preparation comes in tablets of 10 mg. each and may be given to adults in doses of two or three tablets three times a day after meals, provided there are no contraindications, such as hypertension.

INCIDENCE OF MULTIPLE BIRTHS

To the Editor:—Kindly quote the frequency of birth of twins (of the same and the opposite sex), triplets (of the same and the opposite sex) and quadruplets (are there any of the opposite sex or are they always girls?). Is there any record of five and only five fetuses? The Canadian, the Italian and the African were all six fetuses. Kindly give this your immediate attention.

M.D., Pennsylvania.

ANSWER.—A frequently repeated rule concerning the incidence of twins, triplets and quadruplets is Hellen's formula, according to which twins occur once in 80 single births, triplets once in 80^2 births or 1 in 6,400, and quadruplets once in 80^3 births or in 1 in 512,000. Das (*J. Obst. & Gynec. Brit. Emp.* **41**:227 [April] 1934) analyzed statistics concerning 186,842,231 births and found that twins occurred once in every ninety births, the highest proportion occurring in Russia and Denmark (one in seventy-one) and the lowest in Japan (one in 301). However, hospital statistics of fifteen countries showed that twins occurred once in every seventy-nine labors. Twins were more frequently born among the colored population not only in the United States but also in India.

In a series of 803 pairs of twins studied by Orel (*Arch. f. Gynäk.* **129**:719, 1927) 547 were of the same sex and 256 were of the opposite sex, giving a ratio of 68.1 : 31.9 per cent. This author found that single ovum twins occurred in between 23 and 26.6 per cent of all cases of twins and that boys occurred with almost equal frequency in single and double ovum twins. In a study of 717,907 twins, Nichols (*Mem. Am. Anthrop. A.* **1**, 1907) found that both children were males in 234,497, both were females in 219,312 and they were of opposite sex in 264,098.

Triplets may be of single, double or triple ova and they may all be of the same sex or there may be two of one sex and one of the opposite sex.

According to Hellen, quadruplets occur once in 512,000 births, but according to Gruelich (*Am. Naturalist* **64**:142, 1930), who analyzed 120,061,398 pregnancies, quadruplets occurred once in 727,159 deliveries. Quadruplets may be monozygotic, dizygotic, trizygotic or quadrazygotic. They may be all male, all female or of both sexes. Pryor (*Am. J. Anatomy* **59**:409 [Sept. 15] 1936) was able to find only five sets of quadruplets in the United States that have reached the age of 2 years or more.

About thirty cases of quintuplets have been reported. The incidence of this occurrence has been estimated as one in 41,600,000 pregnancies. Dr. Dafoe, who attended the Dionne quintuplets, reported the case in THE JOURNAL, Sept. 1, 1934, p. 673, and he made no mention of a sixth fetus. According to De Lee there is only one authentic case of sextuplets.

LEUKOPLAKIA BUCCALIS

To the Editor:—A man, aged 27, single, noticed six months ago some white smooth milky patches at the tip on the dorsal surface of the tongue, to which he had not given any importance. Three days ago he noticed that these white areas have spread to the middle third of the tongue. Irregular white smooth areas alternating with coarsely infiltrated areas were found on the upper surface of the tongue from the middle third to the tip. On the margins of the organ, cracks and deep rhagades could be plainly seen; on squeezing, no exudation was elicited. On instrumental manipulation, pain is not felt. The blood Wassermann test is negative; the patient has not enough money to pay further diagnostic expenses such as for a spinal fluid Wassermann test. Taste sensitiveness is normal. Tobacco (smoking and chewing) and the liquor habit are not indulged in. There is no evidence of a chancre that may suggest syphilis. I am inclined to diagnosis this case as leukoplakia buccalis despite the emphatic assurance of the patient that he does not use tobacco or liquor. Your opinion with regard to diagnosis and suggestion as to treatment will be deeply appreciated. Please omit name.

M.D., California.

ANSWER.—This case is most probably one of leukoplakia buccalis associated with a scrotal tongue. While a certain number of these cases are associated with syphilis and heavy smoking, it is possible for these to be absent in some cases. Poor hygiene of the mouth, carious teeth, and ingestion of highly seasoned, spiced and hot foods may be contributory factors and should be ruled out. Other conditions that must be considered are lichen planus, which may be limited to the buccal mucosa, but, as a rule, the characteristic angular, violaceous, itching papules are usually present on the flexor aspects of the wrist and about the ankles, with associated lesions on the body. The buccal and tongue lesions usually appear as smooth or fissured plaques, with a tendency to occur in rings having linear striae and covered by a silver white pellicle.

Monilial infection of the tongue must also be considered. In this condition there are usually white, scroll-like patterns, and the area is covered by a shiny, gelatinous, translucent membrane. Microscopically, monilial or other yeastlike organisms are found.

Leukoplakia buccalis is best treated by care to the hygiene of the mouth and teeth, the use of antiseptic mouth washes, and the destruction of any thickened or ulcerated areas by electrocoagulation, radium or carbon dioxide snow.

Lichen planus calls for systemic treatment with mercurials or arsenic by mouth or, preferably, by injection.

Monilial infections are best treated by a saturated solution of gentian violet and the use of a sodium perborate mouth wash.

STERILIZING DIAPERS

To the Editor:—Will you please give me a formula for a chlorine solution for sterilizing diapers? Please give directions for use. Kindly omit name.

M.D., Michigan.

ANSWER.—A chlorine solution for sterilizing diapers is not generally recommended. The chlorine salts are rather strong chemicals, and not only might they be injurious to the fabric of the diaper but they might also irritate the baby's skin if the chlorine solution has not all been removed from the cloth. It has been the practice in bleaching cloth when calcium hypochlorite is used to neutralize with sodium bisulfite after the bleaching process, in order to avoid injury to the material of the cloth.

The simplest and most efficacious method of sterilizing diapers is to wash them well in soap suds, rinse out the suds in clear water and then boil the diapers. After the diapers are dried, preferably in the sun, they may be pressed with a hot iron. In cases of "ammoniacal diapers" it has been recommended that in addition to the routine laundering the diapers

be soaked in a solution of boric acid (two heaping tablespoonfuls of boric acid powder to a quart of water). The diapers are not rinsed after soaking in the boric acid solution but wrung out and dried. Traces of boric acid left in the diaper neutralize ammonia and also retard the growth of bacteria that produce the ammonia.

ATROPHIC ARTHRITIS

To the Editor:—A man, aged 40, had the usual childhood diseases. In 1920 he had a tonsillectomy but a moderate sized tag was left in. In 1921 he was given 1,500 units of tetanus antitoxin for a trivial puncture wound. There was no reaction from the serum. Four years ago he contracted a mild pharyngeal diphtheria for which he was given 10,000 units of diphtheria antitoxin intramuscularly. One week after this he developed a severe serum reaction. There was an intense urticaria lasting for three days. The itching was so intense that it necessitated almost constant bathing with alkalis. Epinephrine gave transient relief. There was swelling of the lips and eyelids and apparently some edema of the glottis, as evidenced by hoarseness and slight difficulty in breathing. Joint symptoms were severe. The urticaria and edema gradually disappeared, but the pain and stiffness in the joints persisted. This was especially noted in the knees when walking was first attempted. The joint symptoms have spread so that there has been involvement of all the joints. There is moderate crepitation on motion in the wrists and in one ankle. The patient has a chronic arthritis of the atrophic type. At the time of the serum reaction the patient had two devitalized but not abscessed teeth; they had been roentgenographed a short time before. He also had the small tag of tonsil previously mentioned. He is of the asthenic type, 71½ inches (182 cm.) in height and weighing about 140 pounds (63 Kg.) at the time of the serum reaction. He was otherwise in good physical condition. At the present time the arthritis seems to be progressing and the joint symptoms are more severe. Foci of infection have been removed but no other therapy has been instituted save for analgesics for pain. Is chronic arthritis a very uncommon occurrence following severe serum sickness? What is the relationship between the serum reaction and the chronic arthritis? Would the patient have been likely to develop an arthritis if he had not had this severe serum reaction? Would you treat this condition any differently than any other case of chronic atrophic arthritis? Please omit name. M.D., North Dakota.

ANSWER.—Serum disease is a definite clinical entity and as represented in this case the injection of tetanus antitoxin provoked the formation of antibodies in the tissues. The second injection of antigen in the diphtheria antitoxin reacted with the preformed antibody resulting in anaphylactic shock.

The inquirer does not mention the presence in the patient of other symptoms of atrophic arthritis beyond pain and stiffness of the joints nor does he indicate the time interval between the anaphylactic reaction and the onset of active joint disturbance, such as swelling or discoloration. Joint pains have been known to persist for quite some time following serum sickness, although serum disease per se is not generally regarded as a cause of atrophic arthritis. What probably happened in this case is that the patient was already "marked" for arthritis and the serum reaction served merely as a precipitating cause. In almost all cases of atrophic arthritis it is possible to discover a precipitating cause, which involves some unusual drain on the patient's resistance and serves to transfer the patient from the prearthritic state into the arthritic state. Among the more common precipitating causes are respiratory infections, surgical operations, childbirth, severe nervous shock and gastro-intestinal upsets.

The treatment of this patient should include the usual measures of recognized benefit in atrophic arthritis. Since calcium is believed to be beneficial in anaphylactic conditions, it might be advisable to give this drug a trial.

DYSCHONDROPLASIA

To the Editor:—Would you please give me whatever information you may have available regarding dyschondroplasia or multiple congenital enchondrosis? I know of such a case in a man, aged 24, involving the left forearm and left lower leg. There is a shortening of the left ulna, and bony exostoses in the left ulna, left scapula and left tibia. The condition has been present since birth. Incidentally, the father and sister of this man suffer from the same condition. Could you give me any opinion as to the prognosis and any possible type of treatment? If this query is published, please omit name. M.D., Wisconsin.

ANSWER.—Dyschondroplasia, with or without exostoses, was so well described by Ollier in 1898 that it has been called by his name. There is no known etiologic factor but its hereditary tendencies have long been recognized. The growth changes are attributed to defects in the primary germ cell and have no relation to any postnatal complications. Only bones that are preformed in cartilage are affected.

Exostoses that cause disturbances of locomotion or function should be removed and deformities may be corrected by osteotomy, but there is no specific treatment that is known at the present time.

EXCESSIVE HIRSUTY IN WOMEN

To the Editor:—A woman, aged 24, single, complains of growth of hair on the face and the chest, male distribution on the abdomen, and moderate growth on the arms and thighs, present since childhood. The menses set in at the age of 13, occur every twenty-eight days, and last four or five days. The pulse is 84, the blood pressure 110 systolic and 70 diastolic, the height 5 feet 3 inches (160 cm.), the weight 108 pounds (49 Kg.), the hemoglobin 65 per cent. The thyroid is slightly enlarged; the extremities are warm. The breasts are well developed and firm. On the ground that the anterior pituitary extract is supposed to produce hair growth in certain alopecias, is it logical to assume that the anterior pituitary body is hyperfunctioning in this case and that the use of an antagonistic gland will produce a disappearance of the excessive growth of hair? What gland is antagonistic to the anterior pituitary? The patient has had occasional right frontal headache during the morning hours, worse in damp weather, for five years. Tonsillectomy was performed five years ago for frequent sore throat. General bodily weakness and a postnasal drip have existed since an attack of sinusitis four years ago. Could an adrenal gland tumor be the causative agent? Is thyroid indicated? No pelvic examination was attempted, since the organs are presumed normal on the basis of normal menses and breast development. Please omit name. M.D., New Jersey.

ANSWER.—Excessive hirsuties in the female may be due to a variety of causes, any one of which or a combination of all may be operative. These may be summed up as follows:

1. An overactive pituitary, particularly the anterior lobe.
2. An adrenal disturbance involving the cortex, usually of the tumor type.
3. A deficiency of ovarian hormones, or certain types of ovarian tumor.
4. An overactive thyroid.

The possible causes will have to be analyzed to determine the basis for the condition.

The question as to which gland is antagonistic to the pituitary is difficult to answer, for the anterior pituitary contains apparently a large number of special hormonic agents, each one of which would have its own antagonist. The whole situation is one that is exceedingly complicated and it actually involves an investigation into the entire endocrine balance.

The unilateral frontal headaches would suggest a pituitary disturbance; the rapid pulse, with an enlarged thyroid, would suggest hyperthyroidism.

A pelvic examination ought to be made if possible to determine the presence or not of an ovarian tumor; an examination of the adrenals should be made for the same purpose. A roentgenogram of the head showing the pituitary fossa and a basal metabolic test should be made.

Nothing has been said about lineae atrophicae, either purple, pink or white, which occasionally appear on the thighs, abdomen or shoulders in these cases; if these are present it would indicate an anterior lobe deficiency allied to the Cushing syndrome.

QUARTZ FRAGMENT IN LENS CAPSULE

To the Editor:—For the past six months a miner has been carrying a piece of quartz, a 1 mm. cube, on the anterior lens capsule of the eye. The symptoms are unilateral diplopia, central "shadow" effect, and prism "rainbow" in bright light. On examination the eye presents no evidence of irritation. There is a small leukoma at the limbus where the foreign body entered and the quartz is clearly visible in the midpupillary zone on the anterior lens capsule, dropping slightly on changing the position of the head but fixed to the lens capsule. As I am unable to find authority in the literature available to me, I should like the following information: 1. If left alone, what is the prognosis? 2. If properly removed now, could one expect an opaque scar in the anterior lens capsule or possibly precipitate a traumatic cataract formation? 3. Is it safer to wait until signs of irritation develop (if any) and only then remove the foreign body? 4. If the quartz should drop off the lens capsule into the anterior chamber in the future, might it scarify the endothelium or even Descemet's membrane sufficiently to impair vision? 5. Kindly cite authority on subject. GEORGE S. WEISS, M.D., Winnemucca, Nev.

ANSWER.—1. If the condition is left alone, it is probable that a complete traumatic cataract will ultimately develop. The reason is that the piece of quartz must be embedded in the anterior lens capsule; otherwise it could not remain in the described position. Consequently there must be a solution of continuity of the capsule. With such a condition there will be a gradual seepage of aqueous into the lens through the capsule rupture and eventual cataract formation (Weiss, O.: Physiology of Nutrition of Eye, Kurzes Handbuch der Ophthalmologie, vol. 11). A few cases have been reported of foreign bodies entering the lens through a minute tear in the capsule, which closed immediately afterward without formation of cataract (Elschnig and others, 1910).

2. Both.

3. It is not probable that there will be any signs of irritation in that eye. As long as the quartz remains in situ and does

not come in contact with the uvea, no inflammation is to be expected. Consequently, removal of the foreign body may be postponed indefinitely.

4. Probably not.

5. There seems to be no record of intra-ocular quartz foreign bodies in the literature and only an occasional reference to foreign bodies that have remained adherent to the anterior lens capsule without penetration. The statements that are made regarding intra-ocular pieces of glass undoubtedly hold true for intra-ocular quartz. For references, see Wagenmann: Injuries (Graefe-Saemisch Handbuch der gesammten Augenheilkunde, edition 2, pp. 1395 and 1399) and Cramer, E.: Injuries (Kurzes Handbuch der Ophthalmologie, volume IV).

MR. ALBERT PAYSON TERHUNE AND THE PHYSIOLOGY OF FEAR

To the Editor:—Will you please inform me whether the following statement by Albert Payson Terhune, which appeared in the *Reader's Digest*, is true: "Do not allow fear to master you when you are in the presence of an ill-tempered or vigilant dog. My reason for stressing this may sound fantastic, yet it is an established scientific fact. When you are frightened, nature pumps an undue amount of adrenalin through your system. This throws off an odor said to be like that of formic acid, which human nostrils fail to detect. Dogs, however, hate it. It rouses some of them to contempt. Many an otherwise inoffensive dog will attack when that odor reaches him." A. J. REICH, M.D., New York.

ANSWER.—Mr. Terhune's advice not to let fear master you is sound, whether you face a dog or any other potential danger, but the reasons given for expression of fear as a factor of safety are, if not fantastic, at least not based on known or proved facts. Intense fear may, indeed, cause some increased secretion of epinephrine. Even this is in dispute. But there is no evidence that increased epinephrine leads to exhalations from the body, exhalations inducing "hate" and "contempt" in the canine species. We know, for a fact, that many hundred times the normal output of epinephrine may be injected intravenously in dogs, and man, in the presence of dogs, with the latter showing no "hate" or "contempt" detectable by man. If and when an otherwise innocuous dog attacks a man in a state of fear, it is probably due to the man's action rather than to his odors. To be sure, a person in great fear may lose control of his sphincters, but the ordinary human nose is not immune to the odors thus released; these odors are not like formic acid, and science knows of no evidence that they induce hate and contempt in pups.

ACIDIFICATION OF URINE

To the Editor:—Recently I have been having difficulty with my patients following transurethral prostatectomy. In spite of the fact that there is no residual urine, the urine remains persistently alkaline, and there is a large amount of triple phosphate and calcium phosphate crystals in the urine. Patients also complain of a great deal of terminal burning and some frequency. The patients experiencing this trouble are mostly from a district where the water is very hard and contains alkali. I have used acid sodium phosphate, ammonium nitrate and ammonium chloride in an attempt to acidify the urine, without success. I would appreciate any suggestion that you could offer for relief of this condition. Kindly omit the name. M.D., South Dakota.

ANSWER.—In all cases in which acidification of the urine is aimed at, an acid-forming diet should be resorted to even prior to or jointly with medication. Such diet includes all animal foods, excepting milk, and all cereals, while fruits and vegetables must be excluded. In resistant cases the ketogenic diet should be resorted to, giving, for example, water flavored with tea and saccharin for two days and adding to this 350 cc. of whipped cream on each of the following three days.

PILONIDAL CYST

To the Editor:—A man, aged 28, has had a pilonidal cyst since 1931. He has had two radical operations, but the sinus has recurred each time and the patient has not improved following the operations. He has consulted some of the best men in the country, who have suggested that the sinus may connect with the spinal canal through the sacral foramina and account for the persistence of the sinus. If it does connect with the spinal canal, what mode of treatment would you suggest? If there is any literature on this subject, kindly give me references. Please omit name. M.D., South Dakota.

ANSWER.—Probably a portion of the cyst still remains. In order to make sure of its extent, the sinus may be injected with thorium dioxide sol 20 per cent. After the injection roentgenograms should be made in both the anteroposterior and lateral positions. This will in all probability outline the exact extent and locality of the cyst.

Only occasionally does the cyst extend into the spinal canal. When this occurs, the cyst must be removed in order to effect a perfect cure. It probably does not come within the subarachnoid spaces.

EFFECTS OF LONG CONTINUED USE OF BARBITURATES

To the Editor:—Mrs. B. G. J., aged 58, has for several years had hypertensive cardiovascular renal disease. When I first saw her about one year ago I prescribed pentobarbital sodium capsules 1½ grains (0.1 Gm.) three times a day for relief of pain. Since that time she has continued to take them, consuming on the average six capsules a day. Aside from the mere habit formation, will you please outline for me the deleterious effects from such a rate of consumption of this drug. Also, what would you suggest that I prescribe to take the place of it? Please omit name. M.D., Texas.

ANSWER.—A search of the literature fails to reveal reports of deleterious effects from such habitual consumption of pentobarbital sodium, though this may be ascribed to the rather recent introduction of the drug than to lack of possibility of their occurrence. Acetylsalicylic acid is an excellent analgesic, acting in a different manner from that of pentobarbital sodium and with well known untoward effects that may be watched for. The gradual substitution of this for the other drug by combining the two in the same capsule may solve the problem.

HEMIATROPHY OF BODY

To the Editor:—I have a patient on whom no laboratory work has been done and I am at a loss as to where to begin. A girl, aged 4½ years, apparently normal in all other respects, has for the past year had an arrested development on the same side, from the shoulder girdle to the hand and from the gluteal region to the foot. The hand and foot are much smaller than those of the opposite side and the muscles of the fleshier parts much wasted. Can you help diagnose this case? Please omit name and address. M.D., Iowa.

ANSWER.—The patient is affected by a condition known as hemiatrophy of the body. At best it is difficult to determine the etiology of this disorder. As a rule it is congenital in origin, though one should not fail to make careful neurologic examination. In some instances hemiatrophies may be traced to a birth injury with a resulting infantile palsy, though in the absence of paralysis, spasticity, other neurologic changes and a carefully obtained history, focal cerebral lesions may be excluded.

DEPRESSIVE PSYCHOSES OF MANIC-DEPRESSIVE TYPE

To the Editor:—Is there any evidence that you know of to show the sexual etiology of the depressive psychoses of the manic-depressive type? Are there any statistics to show that these depressions occur in eunuchs or in women who may have had their ovaries removed in early life? Any data or references you may be able to offer on this particular topic will be greatly appreciated. Kindly omit my name. M.D., New York.

ANSWER.—Depressive psychoses of the manic-depressive type are prone to develop in persons who are constitutionally predisposed to them, under conditions of stress of various kinds. They occur not uncommonly at puberty and the climacteric, particularly the latter, whether it occurs spontaneously or is induced artificially. There is no evidence that eunuchs are particularly prone to them. This, however, does not establish a sexual etiology. The stresses of exhaustion, bodily illness, pregnancy and lactation may also precipitate attacks of depression, and the same is true of emotional stress in reaction to situations in the outside world.

PNEUMONIA FOLLOWING INJECTION OF SERUM

To the Editor:—A man in excellent health punctured his foot on a nail at 8 o'clock in the morning. Two hours after this he received an injection of antitetanic serum and developed, the next day, lobar pneumonia followed by pleural effusion. Is there any connection between the injection of serum he received and the lung reaction he developed? Please omit name. M.D., Canada.

ANSWER.—No.

"OPHTHALMOSCOPIC SIGNS OF DEATH"

To the Editor:—I should like to comment on your reply to Dr. Wyatt Barnes's inquiry about the ophthalmoscopic signs of death (THE JOURNAL, October 24, p. 1408) in which you state that "the interrupted blood column makes its appearance only in the veins." I have seen the blood column interrupted in the arteries at the time of death, and my own experience is corroborated by C. H. Usher (*Ophth. Rev.* **15**: 339, 1896). As a matter of fact, the article quoted as your reference (American Encyclopedia of Ophthalmology **5**: 3784) reads "These interruptions . . . are apparent chiefly in the veins."

GORDON M. BRUCE, M.D., New York.

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BOARDS

ALABAMA: Montgomery, June 29-July 1. Sec., Dr. J. N. Baker, 519 Dexter Ave., Montgomery.

ALASKA: Juneau, March 2. Sec., Dr. W. W. Council, Juneau.

ARIZONA: Phoenix, Jan. 5-6. Sec., Dr. J. H. Patterson, 826 Security Bldg., Phoenix.

CALIFORNIA: *Reciprocity.* Los Angeles, Dec. 16. Sec., Dr. Charles B. Pinkham, 420 State Office Bldg., Sacramento.

COLORADO: Denver, Jan. 5. Sec., Dr. Harvey W. Snyder, 422 State Office Bldg., Denver.

CONNECTICUT: *Basic Science.* New Haven, Feb. 13. *Prerequisite to license examination.* Address State Board of Healing Arts, 1895 Yale Station, New Haven.

DELAWARE: Dover, July 13-15. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniel, Dover.

DISTRICT OF COLUMBIA: Washington, Jan. 11-12. Sec., Commission on Licensure, Dr. George C. Ruhland, 203 District Bldg., Washington.

IDAHO: Boise, April 6. Commissioner of Law Enforcement, Hon. Emmitt Pfost, 205 State House, Boise.

ILLINOIS: Chicago, Jan. 26-28. Superintendent of Registration, Department of Registration and Education, Mr. Homer J. Byrd, Springfield.

IOWA: *Medical.* Des Moines, Dec. 1-3. Dir., Division of Licensure and Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines. *Basic Science.* Des Moines, Jan. 12. Sec., Prof. Edward A. Benbrook, Iowa State College, Ames.

KANSAS: Topeka, Dec. 8-9. Sec., Board of Medical Registration and Examination, Dr. C. H. Ewing, 609 Broadway, Larned.

KENTUCKY: Louisville, Dec. 2-4. Sec., State Board of Health, Dr. A. T. McCormack, 532 W. Main St., Louisville.

LOUISIANA: New Orleans, December. Sec., Dr. Roy B. Harrison, 1507 Hibernia Bank Bldg., New Orleans.

MARYLAND: *Regular.* Baltimore, Dec. 8. Sec., Dr. John T. O'Mara, 1215 Cathedral St., Baltimore. *Homeopathic.* Baltimore, Dec. 8-9. Sec., Dr. John A. Evans, 612 W. 40th St., Baltimore.

MICHIGAN: Ann Arbor and Detroit, June 9-11. Sec., Board of Registration in Medicine, Dr. J. Earl McIntyre, 202-3-4 Hollister Bldg., Lansing.

MINNESOTA: *Basic Science.* Minneapolis, Jan. 5-6. Sec., Dr. J. Charnley McKinley, 126 Millard Hall, University of Minnesota, Minneapolis. *Medical.* Minneapolis, Jan. 19-21. Sec., Dr. Julian F. Du Bois, 350 St. Peter St., St. Paul.

MONTANA: Helena, April 6. Sec., Dr. S. A. Cooney, 7 W. 6th Ave., Helena.

NEW HAMPSHIRE: Concord, March 11-12. Sec., Board of Registration in Medicine, Dr. Charles Duncan, State House, Concord.

NEW MEXICO: Santa Fe, April 12-13. Sec., Dr. Le Grand Ward, Box 693, Santa Fe.

NEW YORK: Albany, Buffalo, New York and Syracuse, Jan. 25-28. Chief, Professional Examinations Bureau, Mr. Herbert J. Hamilton, 315 Education Bldg., Albany.

NORTH CAROLINA: *Endorsement.* Raleigh, Nov. 30. Sec., Dr. Ben J. Lawrence, 503 Professional Bldg., Raleigh.

NORTH DAKOTA: Grand Forks, Jan. 5-8. Sec., Dr. G. M. Williamson, 4½ S. 3rd St., Grand Forks.

OHIO: Columbus, Dec. 2-4. Sec., State Medical Board, Dr. H. M. Platter, 21 W. Broad St., Columbus.

OKLAHOMA: Oklahoma City, Dec. 9. Sec., Dr. James D. Osborn, Jr., Frederick.

OREGON: Portland, Jan. 5-7. Sec., Dr. Joseph F. Wood, 509 Selling Bldg., Portland.

PENNSYLVANIA: Philadelphia, January. Sec., Board of Medical Education and Licensure, Mr. James A. Newpher, Education Bldg., Harrisburg.

PUERTO RICO: San Juan, March 2. Sec., Dr. O. Costa Mandry, Box 536, San Juan.

RHODE ISLAND: Providence, Jan. 7-8. Chief, Division of Examiners, Mr. Robert D. Wholey, 366 State Office Bldg., Providence.

SOUTH DAKOTA: Pierre, Jan. 19-20. Dir., Division of Medical Licensure, Dr. B. A. Dyar, Pierre.

VERMONT: Burlington, Feb. 10-12. Sec., Board of Medical Registration, Dr. W. Scott Nay, Underhill.

VIRGINIA: Richmond, Dec. 9-13. Sec., Dr. J. W. Preston, 28½ Franklin Road, Roanoke.

WEST VIRGINIA: Charleston, March 1. Sec., Public Health Council, Dr. Arthur E. McClue, State Capitol, Charleston.

WISCONSIN: *Basic Science.* Milwaukee, Dec. 19. Sec., Prof. Robert N. Bauer, 3414 W. Wisconsin Ave., Milwaukee. *Medical.* Madison, Jan. 12-14. Sec., Dr. Henry J. Gramling, 2203 S. Layton Blvd., Milwaukee.

WYOMING: Cheyenne, Feb. 1. Sec., Dr. G. M. Anderson, Capitol Bldg., Cheyenne.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Parts I and II.* Feb. 9-11, May 10-12, June 21-23, and Sept. 13-15. Ex. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

SPECIAL BOARDS

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOGY: *Written examination for Group B applicants* will be held in various cities throughout the country, April 17. *Oral examinations for Group A and B applicants* will be given in Philadelphia, June 7-8. Sec., Dr. C. Guy Lane, 416 Marlborough St., Boston.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written* examination will be held simultaneously in different centers of the United States and Canada in December. *Practical* or *clinical* examination will be given in St. Louis in April. Chairman, Dr. Walter L. Bierring, 406 Sixth Ave., Des Moines.

AMERICAN BOARD OF OPHTHALMOLOGY: Los Angeles, Jan. 23. *All applications for this examination must be filed before Dec. 1, and case reports must be submitted before Jan. 1.* Sec., Dr. John Green, 3720 Washington Blvd., St. Louis, Mo.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: Cleveland, Jan. 9. *Only applications received by the Secretary on Dec. 1 or before will be acted upon by the Board.* Sec., Dr. Fremont A. Chandler, 180 N. Michigan Ave., Chicago.

AMERICAN BOARD OF OTOLARYNGOLOGY: Philadelphia, June 7-8. Sec., Dr. W. P. Wherry, 1500 Medical Arts Bldg., Omaha.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York, Dec. 29-30. Sec., Dr. Walter Freeman, 1028 Connecticut Ave., Washington, D. C.

AMERICAN BOARD OF RADIOLOGY: Atlantic City, June 4-6. Sec., Dr. Byrl R. Kirklin, Mayo Clinic, Rochester.

AMERICAN BOARD OF UROLOGY: Chicago, Dec. 4-6. Sec., Dr. Gilbert J. Thomas, 1009 Nicollet Ave., Minneapolis.

Texas June Report

Dr. T. J. Crowe, secretary, Texas State Board of Medical Examiners, reports the written examination held in Austin, June 23-25, 1936. One hundred and eighty-two candidates were examined, 163 of whom passed and 19 failed. One hundred applicants were licensed by endorsement. The following schools were represented:

PASSED		
School	Year Grad.	Number Passed
Northwestern University Medical School	(1936)*	1
Tulane Univ. of Louisiana School of Medicine (1935),	(1936)	2
Johns Hopkins University School of Medicine	(1928)	1
Harvard University Medical School	(1936)	1
Creighton University School of Medicine	(1933)	1
University of Nebraska College of Medicine	(1936)	1
Columbia Univ. College of Physicians and Surgeons	(1933)	1
University of Pennsylvania School of Medicine	(1936)	1
Baylor University College of Medicine....(1935),	(1936, 69)	70
University of Texas School of Medicine..(1935),	(1936, 71)	72
Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin	(1927)†	1
Thüringische Landesuniversitat Medizinische Fakultät, Jena	(1922)†	1
Universität Basel Medizinische Fakultät	(1934)†	1
Osteopaths‡		9

FAILED		
School	Year Grad.	Number Failed
Tulane University of Louisiana School of Medicine	(1935)	1
Jefferson Medical College of Philadelphia	(1934)	1
Baylor University College of Medicine	(1936, 4)	4
University of Texas School of Medicine	(1936, 2)	2
Escuela Médico Militar, México, D. F.	(1922)†	1
Universidad Nacional Facultad de Medicina, México, D. F.	(1936)†	1
Osteopaths‡		8
Nongraduate		1

LICENSED BY ENDORSEMENT		
School	Year Grad.	Endorsement of
University of Arkansas School of Medicine	(1933), (1935, 2)	Arkansas
University of California Medical School	(1934)	Missouri
Emory University School of Medicine	(1931)	Georgia
University of Georgia School of Medicine	(1933)	Georgia
Chicago College of Medicine and Surgery	(1917)	Illinois
Illinois Medical College	(1901)	Iowa
Northwestern University Medical School	(1930) (1931) South Dakota	Illinois,
Rush Medical College	(1926)	Illinois, (1931) Michigan
School of Medicine of the Division of the Biological Sciences	(1935)	Illinois
University of Illinois Col. of Medicine	(1934, 3), (1936, 2)	Illinois
Indiana University School of Medicine	(1929)	Indiana
University of Kansas School of Medicine	(1933)	Kansas
University of Louisville Medical Department	(1910)	Kentucky
University of Louisville School of Medicine	(1935)	Kentucky
Louisiana State University Medical Center	(1936)	Louisiana
Tulane University of Louisiana School of Medicine	(1933), (1935) Alabama, (1929), (1933, 2), (1934, 3), (1935, 2) Louisiana, (1933) Michigan, (1932) Mississippi	
Johns Hopkins University School of Medicine	(1933), (1935)	Maryland
Harvard University Medical School	(1931)	Washington
Tufts College Medical School	(1925)	Mass.
University of Michigan Medical School	(1929, 2)	Michigan
Marion-Sims College of Medicine, Missouri	(1893)	Illinois
St. Louis University School of Medicine	(1913), (1932), (1934) Missouri	
Washington University School of Medicine	(1921) (1932) Missouri	Kansas,
Creighton University School of Medicine	(1932)	California
University of Nebraska College of Medicine	(1923), (1935)	Nebraska
Eclectic Medical College, Ohio	(1928)	Kentucky
Ohio Medical University	(1904)	Ohio
University of Cincinnati College of Medicine	(1932)	Ohio
University of Oklahoma School of Medicine	(1931), (1933)	Oklahoma
Hahnemann Med. College and Hosp. of Philadelphia	(1891)	Illinois
Jefferson Medical College of Philadelphia	(1915)	U. S. Army
Medico-Chirurgical College of Philadelphia	(1916)	U. S. Army
University of Pennsylvania School of Medicine	(1918)	N. Carolina
Meharry Medical College	(1929) (1933), (1934), (1935, 2) Tennessee	Louisiana,
Memphis Hospital Medical College	(1902) (1909) Mississippi, (1911) Oklahoma	Arkansas
Vanderbilt University School of Medicine	(1933)	Tennessee
Baylor University College of Medicine	(1930) Ohio, (1931)	Louisiana
Medical College of Virginia	(1931)	Virginia
University of Toronto Faculty of Medicine	(1921)	Penna.
University of Western Ontario Medical School	(1929)	New York
Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin	(1931)†	New York
Julius-Maximilians-Universität Medizinische Fakultät, Würzburg	(1924)†	Colorado

Regia Università degli Studi di Firenze. Facoltà di Medicina e Chirurgia.....(1928) New Jersey Osteopaths‡ .....Iowa, 4, Georgia, Missouri, 11, Nebraska, Ohio, Oklahoma, 2, Oregon, Pennsylvania, 2, South Dakota

* This applicant has received the M.B. degree and will receive the M.D. degree on completion of internship.
† Verification of graduation in process.
‡ Examined in medicine and surgery.

Book Notices

The Thyroid: Surgery—Syndromes—Treatment. By E. P. Sloan, M.D. Edited by Members of the Sloan Clinic, Guy A. Sloan, M.D., et al. And with a foreword by Wm. Seaman Bainbridge, M.D. Cloth. Price, $10. Pp. 475, with 99 illustrations. Springfield, Illinois, & Baltimore: Charles C. Thomas, 1936.

This work of E. P. Sloan is edited posthumously by the members of his clinic and is divided into twenty chapters. While much of what is stated in discussions on anatomy, physiology and endocrinology are known facts, the question of the etiology of endemic goiter is thoroughly considered. The work of Crotti, of a contagium vivum as the exciting cause of endemic goiter, gives much food for thought. It is pointed out that Crotti's conception is upheld by McCarrison. Iodine insufficiency, mineral imbalance and catalytic agents as possible etiologic factors are scrutinized. The author's hypothesis disagrees with the usually accepted pathogenesis of dysthyroidism. He also offers a classification of the divers types of goiter by dividing its pathology into four main groups, adding a number of subdivisions to each. A survey of preventive measures and the pathology of thyroid disease, as well as symptomatology, diagnosis and prognosis, are ably discussed. The therapeutic aspects of thyroid disease (nonsurgical and surgical) are well handled. In the former the author believes that mineral deficiency as related to thyroid disease is of the "utmost importance" and he recommends the use of sodium phosphate in 20 to 30 grain (1.3 to 2 Gm.) doses three times a day, as advocated by Kocher many years ago. This may be augmented by the use of phosphorus, calcium and sulfur, the last suggested in the form of sulfonated bitumen (ichthammol), with which he has had "unusual success in both toxic and atoxic goiter." On the successes reported by the roentgenologist in the treatment of toxic goiter by means of x-rays, Sloan fails to find "incontrovertible conclusions concerning the efficacy" of such treatment. Twenty per cent of his series of cases were subjected to roentgen treatment previous to coming under his observation; fifty per cent of these patients stated that they were "improved" and, while classed as cured, they have not been "entirely well." The other fifty per cent reported no results from the treatment. An analytic study of the pros and cons of radium treatment is interesting. Commenting on the use of x-rays in intrathoracic goiter, the author says "In this type of goiter harm is done more often than anything else." He recommends its use, however, in malignant disease of the thyroid. Chapter 10 deals with the surgical treatment of thyroid disease. It is an excellent chapter. A comparative study of anesthetics is added. Commenting on basal anesthetics, the author states that the combination of morphine and scopolamine when used in proper dosages produces ideal anesthesia. He adds that "barbital cannot be used with safety for complete anesthesia but for the control of mental states previous to operation." The illustrations and colored plates by William B. McNett are well executed.

While the technical steps of thyroidectomy are standardized perhaps, the author justly remarks that every goiter surgeon has a tendency to develop his technic along certain lines and to introduce little innovations and improvements, but that the author finds that "this [his] fully developed technic is in his hands immeasurably better than any other." The reasons for the various technical steps are carefully discussed and, rather ingeniously, Sloan compares his method of thyroidectomy with obstetric delivery. He speaks of "flexion," "rotation" and "delivery" as pertaining to removal of the thyroid. For completeness of the cycle, the author may as well have compared dividing the prethyroid structures as "rupture of the membranes" and exposure by retraction as "dilation." The complications arising during thyroidectomy and their treatment are succinctly described. The chapter on postoperative management contains many valuable hints on the avoidance of complications and how to steer the patient through postoperative thyrotoxic crises. The chapter on the parathyroid and thymus glands are no less thorough than are the others. The final two chapters on the history, nomenclature and classification afford much information and interesting reading. The former traces interest in diseases of the thyroid to the pre-Christian era, thence down to the present, and from pioneers to contemporary thyroid surgeons. As especially prominent in thyroid work in America are mentioned Halsted, Rogers, Ochsner, Mayo and Crotti. In speaking of the last named, he calls attention to the fact that Crotti in 1917 published "the first comprehensive treatise on diseases of the thyroid. The effect of this book upon the development of the modern conception and treatment of thyroid disease is hard to evaluate. In this classical treatise he brought together all the worthwhile thought and all the investigations which had been done up to that time and by making this knowledge accessible the appreciation of the importance of the goiter problem was enhanced." A thorough bibliography completes the work. All in all the book is interesting, is well written and contains a vast amount of information.

Studies on the Aetiology and Pathogenesis of Cataracta zonularis. By Gunnar von Bahr, Med. Lic., GBG. An Academic Treatise Which by Due Permission of the Most Experienced Faculty of Medicine at Uppsala Will be Publicly Defended in the Lecture Room of the Physiological Institution Saturday, May 23rd, 1936, 10 A. M., to Obtain the Degree of Doctor of Medicine. Paper. Pp. 240, with illustrations. Uppsala: Almqvist & Wiksells Boktryckeri-A.-B., 1936.

This is an academic treatise which "by due permission of the most experienced Faculty of Medicine at Uppsala will be publicly defended in the lecture room on May 23, 1936, to obtain the degree of Doctor of Medicine." The author reviews all that is known about cataracta zonularis or capsulolenticularis arida siliquata or perinuclearis from the first description in 1800 to date. This occupies exactly half of the book. The remainder is devoted to the technic and results of rat feeding experiments in the production of congenital zonular cataract. The work is good, and definite conclusions can be drawn that the lenticular opacities result in animals in which experimental rickets is complicated with tetany. The condition apparently causes an injury to the superficial lens fibers with the resultant slow development of the cataract, even though the tetany may disappear. This conclusion is not entirely new, as much of this work has been done previously by others; but von Bahr's work corroborates much of the earlier work and allows of a clear exposition. The bibliography, comprising fourteen pages, is complete. The last four pages are actual photographs of the experimental animals and do not show much. There is nothing revolutionary or excitingly new in all this, but the book does represent careful conscientious work and is praiseworthy. Would that there were more pieces of work of this type emanating from the younger men in this country.

The Comparative Anatomy of the Nervous System of Vertebrates, Including Man. By C. U. Ariëns Kappers, M.D., Sc.D., LL.D., Director of the Central Institute of Brain Research, Amsterdam, G. Carl Huber, M.D., Sc.D., and Elizabeth Caroline Crosby, Ph.D., Associate Professor of Anatomy in the University of Michigan. Volumes I and II. Cloth. Price, $16, per set. Pp. 864; 865-1845, with 710 illustrations. New York: Macmillan Company, 1936.

An appraisal of this great work requires first some reference to its authors and its historical setting. Ariëns Kappers, a pupil of Edinger and during the past twenty-five years director of the Central Institute of Brain Research at Amsterdam, has devoted his whole life to investigation of the comparative anatomy of the nervous system. This program was broadly conceived, was followed with industry and acumen, and has now reached its natural consummation in a comparative investigation of the human brain from the standpoint of its evolution and racial characteristics. In 1920 and 1921 he published in two massive volumes his Die vergleichende Anatomie des Nervensystems (Haarlem, de Erven F. Bohn), which has remained the only comprehensive reference book in this field.

Ten years ago, when Dr. Ariëns Kappers wished to reissue this work in English, in his search for a collaborator he naturally turned to Dr. Crosby, whose thorough familiarity with the field and fidelity to high ideals of accuracy and fitness gave

promise of preeminent qualifications for the task. In this he was not disappointed, for she did the work of translation and rewriting to bring the material down to date so acceptably as to win respect and admiration. Here one can speak without qualification, for in a letter to the reviewer Ariëns Kappers writes "The part Dr. Crosby had in this work is by far the greatest. I hope this will be realized wherever this book is used." It is a pleasure to record in this connection that her own university has recently promoted Dr. Crosby to full professorial rank.

During the progress of this work the late Dr. Huber joined the staff and his ripe scholarship, editorial experience and exacting standards of scientific and literary excellence contributed much to the success of this remarkable achievement. The proficiency of the publishers should not pass without comment, for, despite an unexpected combination of difficulties, they have produced an unusually good example of book making.

The product of this collaboration is a serviceable summary of the best research in the field covered, a summary which is greatly needed, for much of this literature is in relatively inaccessible publications and all of it is technical and hard for the human neurologist to assimilate. It is strictly comparative. The human brain is adequately treated from this standpoint; that is, each region is considered in its comparative and phylogenic relationships. There is no systematic description of it as a whole, for this is available in other manuals. For the same reason there is little reference to the extensive literature on brain weights and measurements, racial differences and other neurologic aspects of physical anthropology, to which Ariëns Kappers himself has recently contributed so extensively. Summaries of these topics are given in his shorter work, The Evolution of the Nervous System in Invertebrates, Vertebrates and Man (Haarlem, 1929).

The first chapter, on the evolution and morphology of nervous elements, is more heavily weighted with theory than any other part of the work. The other chapters, however, are not mere compilations of descriptive details, for the authors everywhere look for general relationships and do not hesitate to advance their own theoretical interpretations. Chapter II is devoted to the spinal cord from Amphioxus to man (pp. 135-334); chapter III to taste and the general afferent systems of the medulla oblongata (pp. 335-432); chapter IV to the lateral line and acoustic systems (pp. 433-515); chapter V to the effectory systems of the medulla oblongata and midbrain, with illustrations and discussion of Ariëns Kappers' principle of neurobiotaxis (pp. 516-644); chapter VI to the coordinating apparatus of medulla oblongata and midbrain (pp. 645-695), and chapter VII to the cerebellum (pp. 696-864). These seven chapters comprise volume I.

In volume II, chapter VIII embraces the mesencephalon and diencephalon (pp. 865-1239); chapter IX the telencephalon, except neopallium (pp. 1240-1516), and chapter X the development of the cortex in mammals (pp. 1517-1713). The last chapter is of especial interest to students and practitioners of human neurology, for here at the culmination of the evolutionary series are fully illustrated discussions of the evolution of fissural patterns, cortical lamination, and patterns of anatomic and physiologic localization.

The work is well documented, and extraordinary care has been taken to ensure the accuracy of these references. The bibliographies appended to the chapters comprise a total of 272 pages, and these judiciously selected titles include most of the significant literature. The index of 131 pages lists every reference to each author and topic treated. The printing is clean and few misprints have been noted, though there are some lapses, as on page 1660, where the citation of figures 636, 640 and 641 refers to the German text of 1921 and should read figures 709 and 710 of the present text. On page 852 the entry C. J. Herrick, 1895, should be C. L. Herrick, and on page 1280 Lepidosteus is referred to as a dipnoan. Figure 423 (fig. 408 of the German text) is based on a crude diagram of the median section of the brain of Amblystoma published by Herrick in 1910. It is unfortunate that the errors of this sketch are perpetuated in the revision, for more accurate figures are now available. In the chapter on the cerebellum the fundamental work of Larsell is not adequately recognized, perhaps because his papers on its morphology and development in lower mammals appeared after this text was completed. Larsell's researches have clarified the morphology of the cerebellum on the basis of more detailed and critical comparative analysis than has heretofore been made.

The blemishes noted are of minor importance in comparison with the general excellence and accuracy of the whole. This is really a new work, not merely a translation and revision of the old. It is indispensable to every serious student of the vertebrate nervous system, for there is no comparable manual in any language, and it will doubtless remain the standard book of reference in this field for many years to come.

Voprosy entsefalografii v detskom vozraste. S prilozheniem atlasa, risunkov i entsefalogramm. Pod redaktsiey S. A. Reynberga. [Problems of Encephalography in Childhood, with Atlas, Drawings and Encephalogram.] Cloth. Price, 6 rubles. Pp. 107, with 137 illustrations. Leningrad: Ogiz-Biomedgiz, Leningradskoe otdelenie, 1936.

The problems of encephalography are presented in the form of essays emanating from the Leningrad Clara Zetkin Scientific-Experimental Institute of Mother and Child Welfare. Since 1929, 170 children have been subjected to the encephalographic method of study at the institute. In fifteen cases the roentgenologic data were controlled by necropsy. There is a chapter by M. A. Toporkova on the technic of the method and a description of an original head bandage in the form of a loop. In a chapter by D. S. Lindenbraten the reader will find a detailed anatomic study of roentgenologic presentation of the brain and its coverings. The approach to the interpretation of encephalograms in pathologic conditions is based on the study of the normal as gleaned from numerous observations of normal brains of children. Two papers by Lindenbraten and H. H. Keler present a combined roentgenologic and clinical study in the various disorders of the brain and the meninges. They present clinical-roentgenologic syndromes of postmeningitic and postencephalitic processes, birth trauma, tumors, microcephaly, cerebral hemiplegia, hydrocephalus and a few of the rarer diseases. The authors made encephalographic studies in seventy-three cases of epilepsy. They emphasize the lack of parallelism between the clinical signs and roentgenograms. An atlas of drawings and encephalograms is appended. This collection of essays because of considerable material and careful study should prove of interest to the pediatrician and the roentgenologist.

Vascular Disorders of the Limbs Described for Practitioners and Students. By Sir Thomas Lewis, C.B.E., F.R.S., M.D., Physician in Charge of Department of Clinical Research, University College Hospital, London. Cloth. Price, $2. Pp. 111, with 5 illustrations. New York: Macmillan Company, 1936.

This excellent volume is written by an internationally known authority who has written eight volumes previously, dealing chiefly with circulation. Most of the material is from papers by the author and his associates, previously published in *Heart* and in the first two volumes of Clinical Science. The absence of controversial data and of a bibliography greatly lessens the value of the book, which is clearly a presentation of the author's explanations and opinions. He admits frankly in the preface that the book is not a comprehensive account of vascular disorders of the limbs. Since several arterial diseases and diseases of the veins and lymphatics are not considered, the title of the volume is somewhat misleading. The author states in the preface that "the time is opportune to attempt to outline conceptions of certain peripheral disorders of the circulation in a way that may prove useful to those engaged, not in research, but in practice." There is grave doubt that the volume will serve this purpose, since diagnosis and treatment are presented incompletely and inadequately. Almost the entire presentation is that of a clinical physiologist interested in mechanisms rather than in diseases.

The chapters on the circulation in the limb and its testing and on the effects of circulatory arrest are excellent. In the chapter on embolism and thrombosis of the main arteries the origin of emboli in the extremities from arteries, particularly the aorta, is overlooked and the explanation of the marked diminution in circulation following arterial embolism is not convincing. Certainly the effects of embolism on circulation are more profound than those of simple ligation or compression of an artery, and this needs further consideration. In the section on the treatment of arterial embolism, methods of increasing collateral circulation are incompletely presented. The short chapter on "postischemic contracture; intermittent claudication"

appears complete, but the thirteen pages on "arteriosclerosis; thrombo-angiitis obliterans" are deficient in many regards. The chapters on "vasoconstriction; local arterial spasm" and on "spasmodic arterial obstruction; Raynaud's phenomenon" are clearly and concisely written. However, the explanation of the uniformly good results that follow sympathectomy for Raynaud's disease of the lower extremities in contrast to occasional failure of good results to follow sympathectomy for Raynaud's disease of the upper extremities is not convincing. Recent investigative work on this problem is not mentioned. The author believes that Raynaud's disease is a manifestation of local fault in digital arteries and that it is not attributable to overactivity of the sympathetic nervous system. His extremely fair attitude toward sympathectomy for Raynaud's disease is conspicuous, for he writes: "Belief or disbelief in the theory that the malady is due to overaction of the sympathetic should not be allowed to weigh for or against operation. The justification of the treatment is to be founded upon experience and not upon theory." The chapter on "gangrene (bilateral forms; cervical rib; general)" is excellent, but the one on "vasodilatation; flushing" leaves much to be desired. It is quite clear that much remains to be done in this field. The term "erythrocyanosis" is used in place of the commonly used terms "cutis marmorata" or "livedo reticularis" but does not appear to be a better designation. The reader may question the accuracy of the statement that "it came in with short skirts and thin stockings and will go out with them." Objection is given to the term "erythromelalgia," and "erythralgia" is suggested as more appropriate. Since the term "erythralgia" is not even included in a standard medical dictionary and since "erythromelalgia" is an accepted medical term, it seems advisable to retain it. Trial of sympathectomy is recommended for this malady, but no reason is given for this recommendation and no results are mentioned. Sympathectomy appears illogical, since pain in this condition is aggravated by increasing the temperature of the skin, an inevitable result of sympathectomy. The final chapter, on vascular disorders in diseases of the nervous system, is clearly written and contains much valuable information.

This book is a superb volume of explanations of mechanisms of circulatory disturbances, although it is of little value to the physician whose chief interests in peripheral vascular diseases are diagnosis and treatment. It is heartily recommended to every student of vascular diseases, since within its covers are to be found explanations of many of the puzzling phenomena observed in abnormalities of peripheral arterial circulation. It is the sort of book which can be read more than once with pleasure and referred to on numerous occasions with profit.

Security Against Sickness: A Study of Health Insurance. By I. S. Falk. Cloth. Price, $4. Pp. 423. Garden City, New York: Doubleday, Doran & Company, Inc., 1936.

This study is predicated on the assumption that some plan for prepayment of sickness costs is necessary to enable certain groups of the population to obtain medical care. The author, who was the associate director of study on the administrative staff of the Committee on the Costs of Medical Care, claims that it was unfortunate during the depression years that "no program of sufficient scope was developed in this period to deal adequately with the major problems or even to hold the promise of effective action on a large or national scale." The author states that the studies represented in part in this volume, undertaken in 1933, were to seek out the principles on which constructive action should rest particularly with respect to certain problems that arise out of illness and its social and economic sequelae. Much of the statistical material is drawn from or is a restatement of the statistics contained in the reports of the Committee on the Costs of Medical Care. Material published by individuals and organizations committed to the the adoption of some form of state managed medicine is used freely. Part two of the study is devoted to a review of the compulsory sickness insurance systems in Germany, France and Denmark and the compulsory health insurance in Great Britain. The reader gathers the impression from the discussion of these foreign systems that the author is disclosing these facts for the first time. The discussion of the statistics of the German system omits comments on the reduction in the amount of demanded medical service with the fall of the value of the mark and omits other interpretations of the German statistics which would have made the discussion more fair and valuable. The author presents the basis of an American program in part three. In the nineteen fundamental principles which the author has formulated as the essentials for an American system, he has endeavored to amalgamate into one program the tenets of the proponents of state managed medicine and some of the objections of those who oppose such a system. Nowhere in these principles is it recognized that food, clothing and housing are sometimes of greater importance to the individual than medical care. This study gives a definite impression that it is an effort to revive or to extend the pronouncements contained in the Majority Report of the Committee on the Costs of Medical Care. The twelve appendixes contain reports, statements of principles and official actions of various groups on the subjects of medical and hospital service. It appears that these quotations are included only for reference. The study itself contains in 361 pages a renewed effort to establish in the United States a system of state managed medicine.

Etude de l'influence des glandes endocrines sur le squelette. Par le Docteur G. Coryn. Vol. XI, Fasc. 1-2, Archives internationales de médecine expérimentale. Publiées par R. Bruynoghe, professeur d'hygiène et de bactériologie à l'Université de Louvain, et A. P. Dustin, professeur d'anatomie pathologique à l'Université de Bruxelles. Paper. Pp. 403, with 94 illustrations. Liége: Imprimerie H. Vaillant-Carmanne, S. A., 1936.

This is in reality a monograph which adequately reviews the pertinent literature referable to the influence of the endocrine glands on the skeleton. The author takes up in order the hypophysis, the sex glands, the parathyroid gland, the thyroid and the adrenals. He has included in each chapter critical analyses of the subjects reviewed and has included case reports that illustrate the conditions under discussion. This is one of the most comprehensive reviews which has appeared in a voluminous literature on this and related subjects during the past decade. For all who are interested, both because of the content of the text and because of the excellence of the bibliography, the book is recommended.

Preventive Medicine. By Mark F. Boyd, M.D., M.S., C.P.H., Member of Regular Field Staff, International Health Division of the Rockefeller Foundation. Fifth edition. Cloth. Price, $4.50. Pp. 561, with 155 illustrations. Philadelphia & London: W. B. Saunders Company, 1936.

New editions of this book have succeeded each other at fairly regular intervals of three to five years since the original publication in 1920. The last previous edition was in 1932, since which time, according to the preface, many sections, including those on colds, ringworm, psittacosis, diphtheria, encephalitis, poliomyelitis, pneumonia, tuberculosis, malaria, typhus and relapsing fever have been either wholly revised or newly written. Recent developments in sewage treatment are noted, and sections dealing with mottled enamel and the rat from a public health standpoint have been added. More extensive consideration is given to the vitamins, silicosis and recent data relating to general morbidity. This edition retains the characteristics of previous editions in being easily readable and carrying a high degree of accuracy. It illustrates, however, in the section on the epidemiology of the amebic dysentery outbreak of 1933 in Chicago, the difficulty inherent in keeping any textbook thoroughly up to the minute. This section already needs revision. The continued demand for the book and the sustained quality of its contents are sufficient evidence of its practicability especially as an introduction to the subject of preventive medicine.

Birth Control Laws: Shall We Keep Them, Change Them or Abolish Them. By Mary Ware Dennett. Cloth. Price, $2.50. Pp. 309. New York: Frederick H. Hitchcock, 1936.

This book is obviously propaganda for the removal of federal and state restrictions on the importation, manufacture and distribution of devices and materials wherewith to prevent conception and for the removal of restrictions on the dissemination of information concerning the prevention of conception. It was copyrighted in 1926 and bears no evidence of having been changed since that date. Those who are interested in the ten-year old views of the lay authoress concerning the development of restrictive legislation in the field of contraception, and concerning the status and future of such legislation ten years ago, may find the book interesting.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Cancer of Breast Allegedly Due to Trauma.—The plaintiff, a tenant in an apartment building, sued the executrix of the owner of the building for personal injuries sustained as a result of an explosion of a hot water system. From a judgment of $30,000 in favor of the plaintiff, the defendant appealed to the Supreme Court of Missouri, division 1, and contended, among other things, that the damages awarded were excessive.

The evidence showed that the plaintiff received fractures of her right arm, both ankles, and her skull; that she sustained severe first, second and third degree burns on her arms, neck, shoulders and back, which left residual scars; that she had impairment of function of her right hand and wrist as a result of the fracture of that arm, and that she would always suffer from headaches and dizzy spells as the result of her skull fracture. In addition to these injuries, a cancer developed in her left breast which her medical testimony tended to show was the result of trauma and due to injuries received in the explosion. She underwent three operations for the removal of the cancerous growths and finally had to have her entire breast and part of her pleura removed. The medical testimony further showed that more cancerous growths had developed which could not be removed because they were too near her lung and that they would ultimately cause her death. It was further shown that at the time of the explosion she was 29 years of age and was in good health. The Supreme Court, while it did not decide whether or not the cancer was due to trauma, held that it was proper for the jury to consider this testimony in fixing the amount of damages. The court concluded that the damages were not excessive.—*Vitale v. Duerbeck (Mo.), 92 S. W. (2d) 691.*

Conjunctivitis from Soot as an Occupational Disease.—The plaintiff, during the course of his employment, was required to cut holes in chimneys as an incident to the installation of gas burning appliances. As he was cleaning the débris from the chimneys, soot would get on his hands, arms, and shirt sleeves. Habitually he would wipe perspiration from his face with his hands and sleeves. After working about a month, his eyes began to smart and, suspecting the soot as the causal factor, he notified his boss, who apparently minimized the probability that the soot had anything to do with the smarting of the eyes. The eye condition grew progressively worse, acute conjunctivitis developed in his left eye, and, in spite of medical treatment, the upper eyelid turned inward so that the eyelashes scraped the eyeball, necessitating an operation for the removal of part of the lid. After the operation, his eyes continued to trouble him more or less, especially on cold days, when there would be excess lacrimation and blurring of vision in both eyes. The plaintiff brought a common law action for damages against the company, and the Kansas City court of appeals, in a divided opinion, affirmed the judgment of the trial court for the plaintiff. (79 S. W. [2d] 1063.) On the request of the dissenting judge, however, the case was certified to the Supreme Court of Missouri, division 2.

The Missouri workmen's compensation act, at the time this cause of action arose, excluded from its operation occupational disease in any form. The principal issue in this case was whether the employee's injury resulted from an occupational disease or from an accident within the meaning of the workmen's compensation act. If the injury resulted from such an accident, then the present common law action was not maintainable, the workmen's compensation commission having original jurisdiction of the case. The question of what constitutes an occupational disease, said the Supreme Court, was discussed at length in *Wolf* v. *Mallinckrodt Chemical Works,* 336 Mo. 746, 81 S. W. (2d) 323 (abstracted in THE JOURNAL, Dec. 7, 1935, p. 1940), in which it was held that combined sclerosis, under the facts in the case, was not an occupational disease because the plaintiff had failed to show that it was peculiar or incident to employment. In the present case there was expert testimony which tended to prove that soot from coal smoke contained an amount of caustic substances sufficient to irritate a person's eye and that repeated injections of soot into the employee's eyes in the manner testified to by him could have produced the injurious consequences of which he complained. Both in the Wolf case and in this case the evidence showed that the condition complained of could have resulted from other causes, not connected with the occupation in question. Likewise, in both cases there was no evidence that any person had ever suffered a similar trouble growing out of a similar occupation. In the present case there was no evidence to show that the employee's trouble was "peculiar and incident to the work or process" or that it was "a disease contracted in the usual and ordinary course of events, which, from the common experience of humanity, is known to be incidental to a particular employment."

The employee's evidence not only failed to show that the injury or disease was peculiar and incident to the work carried on or that it was contracted in the usual and ordinary course of events incidental to his employment, but it showed that it was in the nature of an accident. The employee did not get the soot in his eyes as a usual concomitant or result of the work he was doing, as where one breathes dust laden atmosphere in his working place. He got it on his hands in the ordinary course of his work, but it was communicated to his eyes by his own thoughtless act in wiping sweat from his face with his soot covered hand. He knew each time that occurred, because each time he felt the smarting sensation in his eyes. Had it occurred but once, or a few times within a short period, and resulted in injury, there could be no doubt that it would properly be denominated as an "accident" within the meaning of the workmen's compensation act. The producing cause of the injury in this case did not occur, however, at one time or within a few days, but, by what may be denominated a series of similar accidental occurrences, over a period of four or five weeks. The employee first felt the smarting in his eyes when he had been at work three or four weeks. When he had been working about two months his eyes became sore. This was an unexpected and unforeseen event. The event happened suddenly because, even though the infection was gradual through a period of four or five weeks, instead of a single accidental injury, there was a series of accidental injuries culminating in the same consequential result. The Supreme Court concluded, therefore, that the employee had sustained an accidental injury within the meaning of the workmen's compensation act and that therefore a court of law lacked jurisdiction over the case. The judgment for the employee was consequently reversed.—*Downey v. Kansas City Gas Company (Mo.), 92 S. W. (2d) 580.*

Society Proceedings

COMING MEETINGS

American Academy of Orthopedic Surgeons, Cleveland, Jan. 11-13. Dr. Philip Lewin, 104 South Michigan Blvd., Chicago, Secretary.

Eastern Section, American Laryngological, Rhinological and Otological Society, Boston, Jan. 7. Dr. D. C. Jarvis, Quarry Bank Bldg., Barre, Vt., Chairman.

Middle Section, American Laryngological, Rhinological and Otological Society, Chicago, Jan. 11. Dr. Alfred Lewy, 25 East Washington St., Chicago, Chairman.

Mid-Western Section, American Laryngological, Rhinological and Otological Society, Chicago, Jan. 11. Dr. Frederick A. Figi, 436 Tenth Ave., S.W., Rochester, Minn., Chairman.

National Society for the Prevention of Blindness, Columbus, Ohio, Dec. 3-5. Mr. Lewis H. Carris, 50 West 50th St., New York, Managing Director.

Puerto Rico, Medical Association of, San Juan, Dec. 18-20. Dr. Dolores M. Pinero, Ave. Fernandez Juncos, Parada, 19, Santurce, Secretary.

Radiological Society of North America, Cincinnati, Nov. 30-Dec. 4. Dr. Donald S. Childs, 607 Medical Arts Building, Syracuse, N. Y., Secretary.

Society for the Study of Asthma and Allied Conditions, New York, Dec. 5. Dr. W. C. Spain, 116 East 53d St., New York, Secretary.

Society of American Bacteriologists, Indianapolis, Dec. 28-30. Dr. I. L. Baldwin, College of Agriculture, University of Wisconsin, Madison, Wis., Secretary.

Southern Section, American Laryngological, Rhinological and Otological Society, Memphis, Tenn., Jan. 13. Dr. Charles D. Blassingame, Physicians and Surgeons Bldg., Memphis, Tenn., Chairman.

Southern Surgical Association, Edgewater Park, Miss., Dec. 15-17. Dr. E. Alton Ochsner, 1430 Tulane Ave., New Orleans, Secretary.

Texas Ophthalmological and Oto-Laryngological Society, Fort Worth, Dec. 4-5. Dr. Kelly Cox, 1719 Pacific Ave., Dallas, Secretary.

Western Surgical Association, Kansas City, Mo., Dec. 11-12. Dr. A. H. Montgomery, 122 S. Michigan Blvd., Chicago, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to Fellows of the Association and to individual subscribers in continental United States and Canada for a period of three days. Periodicals are available from 1926 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 12 cents if two periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them. Titles marked with an asterisk (*) are abstracted below.

Alabama Medical Association Journal, Montgomery

6: 125-156 (Oct.) 1936

Practical Application of Physiologic Principles in Treatment of Fractures. W. C. Campbell, Memphis, Tenn.—p. 125.
Clinical Study of Intestinal Obstruction. P. P. Salter, Eufaula.—p. 134.
Ainhum (Dactylolysis Spontanea): Case Report with Roentgenologic and Pathologic Findings. R. H. Alldredge, Fairfield.—p. 137.

American Journal of Pathology, Boston

12: 573-800 (Sept.) 1936

*Nature and Significance of Structural Changes in Lungs in Mitral Stenosis. F. Parker Jr. and Soma Weiss, Boston.—p. 573.
Evolution and Involution of Prostate Gland. R. A. Moore, New York. —p. 599.
Certain Cytoplasmic Inclusions of Liver Cells. A. M. Pappenheimer and J. J. Hawthorne, New York.—p. 625.
Relation of Age and Hypertension to Structure of Small Arteries and Arterioles in Skeletal Muscle. F. C. Andrus, Minneapolis.—p. 635.
Microtechnical Demonstration of Iron: Criticism of Its Methods. G. Gömöri, Budapest, Hungary.—p. 655.
Regeneration of Autoplastic Splenic Transplants. D. Perla, New York. —p. 665.
*Meningococcic Myocarditis. O. Saphir, Chicago.—p. 677.
Relation of Diet to Occurrence of Gastric Lesions in Rat. E. L. Howes, New Haven, Conn., and P. J. Vivier, Johannesburg, Union of South Africa.—p. 689.
Amyloidosis of Lungs and Heart. H. W. Ferris, New York.—p. 701.

Structural Changes in Lungs in Mitral Stenosis.—To ascertain the significance of pulmonary and vascular lesions in mitral stenosis, Parker and Weiss studied nine cases of mitral stenosis of rheumatic origin. The lesions in the pulmonary vessels consisted of intimal thickening of the arteries and hyperplastic arteriolar sclerosis and arteriolar necrosis. The changes in the alveolar walls were marked dilatation of the capillaries, increase in the thickness of the capillary basement membrane, increase in the interstitial tissue (collagen), interstitial pericapillary edema and a tendency of the flat epithelial cells to become cuboidal in shape. The normal thickness of from 1 to 3 microns of alveolar tissue through which oxygen and carbon dioxide have to diffuse can increase up to a thickness of from 30 to 50 microns. Even in the presence of an advanced degree of thickening of the alveolar wall and of the capillary basement membrane, the alveolar basement membrane remains normal. With progressive pulmonary engorgement, first the visible capillaries increase in number, and only later do they dilate. Often the capillaries become displaced and are separated from the alveolar surface by a considerable degree of edema or by thick layers of collagen. Pericapillary and intra-alveolar edema frequently develop independently. Permanent structural alterations in the lungs caused by circulatory failure interfere with the gaseous exchange. In the causation of the pulmonary arterial and arteriolar lesions, an important part is played by the prolonged combined presence of high intravascular pressure, stagnation of blood flow and edema. The similarity between the clinicopathologic syndrome of pulmonary hypertension with malignant sclerosis and advanced cases of mitral stenosis is pointed out.

Meningococcic Myocarditis.—Saphir emphasizes the occurrence and the clinical and pathologic significance of meningococcic myocarditis and reports two fatal cases. Both patients (two of ten) showed meningococcic meningitis. In the first case the culture of the cerebrospinal fluid remained negative. The short stay (two days) of the patient in the hospital prevented obtaining another specimen. Smears from the cerebrospinal fluid, however, showed the characteristic gram-negative intracellular biscuit shaped diplococci. Because of this and the presence of the intracellular gram-negative diplococci in the inflammatory lesions of the myocardium, it seems clear that the cause of the myocarditis was a meningococcic bacteremia, even though absolute proof is missing. In the second case a pure culture of meningococcus was obtained from the cerebrospinal fluid, in addition to finding the organism in the smears from the cerebrospinal fluid and in the sections of the cardiac muscle. Histologically the myocarditis is characterized by hemorrhagic exudate, the early appearance of large endothelial leukocytes, the early destruction of muscle fibers and the presence of intracellular gram-negative diplococci. The foci of necrosis are similar to those seen in the myocardium in instances of subacute bacterial endocarditis. Although in both hearts the lesions were more or less diffuse, the bundle of His was involved, showing polymorphonuclear leukocytic infiltrations and hemorrhage. In view of the prevailing opinion that the primary lesion in meningococcic meningitis is a meningococcic bacteremia (Herrick), it is not surprising that occasionally meningococci may be the cause of an isolated myocarditis. It is likely that the associated myocarditis with resulting myocardial failure seriously influences the prognosis, not only because of the impending myocardial failure but also because it seems that the myocarditis is the result of an overwhelming infection with meningococci. The abrupt death of the first patient may be explained by the overwhelming infection with meningococci, resulting in myocarditis.

American Journal of Psychiatry, New York

93: 249-502 (Sept.) 1936

Control of Behavior, Its Mechanism and Evolution. C. J. Herrick. —p. 249.
Neuroses and Neuropsychoses: Relationship of Symptom Groups. A. Myerson, Boston.—p. 263.
Petit Mal in Children. R. C. Hamill, Chicago.—p. 303.
*Prognosis in Psychoses Lying Midway Between Schizophrenia and Manic-Depressive Psychoses. R. C. Hunt and K. E. Appel, Philadelphia.—p. 313.
Speaking of Weir Mitchell. B. R. Tucker, Richmond, Va.—p. 341.
Psychiatric Hospital Therapy Designed to Meet Unconscious Needs. W. C. Menninger, Topeka, Kan.—p. 347.
Hematoporphyrin Therapy in Affective Psychoses. E. A. Strecker, H. D. Palmer and F. J. Braceland, Philadelphia.—p. 361.
John Addington Symonds: Case: Study in Esthetic Homosexuality. L. J. Bragman, Binghamton, N. Y.—p. 375.

Psychoses Lying Between Schizophrenia and Manic-Depressive Psychoses.—Hunt and Appel observed thirty patients with an even mixture of schizophrenic and manic-depressive features. Of these, eleven recovered and remained well, six recovered and had one recurrence followed by recovery, three recovered but had two or more recurrences and ten were unrecovered, never having a remission, for the most part going on to definite schizophrenia. The recovery rate is therefore roughly twice as good as it is said to be in schizophrenia and from 25 to 50 per cent poorer than that found in pure manic-depressive psychosis. The factors common to the group as a whole were early age of onset, neuropathic heredity, mixed cycloid and schizoid personality traits, a rather high incidence of somatic factors in the illness, a serious precipitating factor in more than half, and a high incidence of persecutory trend, somatic preoccupation and hallucinations.

American Journal of Public Health, New York

26: 961-1070 (Oct.) 1936

Sylvatic Plague Committee. K. F. Meyer, San Francisco.—p. 961.
Study of Pollution of Shellfish Producing Area. A. P. Miller, New York.—p. 970.
Laboratory Problems in Control of Meningococcic Meningitis. R. L. Laybourn, Topeka, Kan.—p. 979.
Interstate Sanitation Compact and Its Implications. C. A. Holmquist, Albany, N. Y.—p. 989.
Need for Training Facilities for Public Health Personnel in the Western States. F. T. Foard, San Francisco.—p. 996.
Staphylococcus Bacteriophage Toxoid: Improved Staphylococcus Antigen. A. Holm, J. F. Anderson and G. F. Leonard, New Brunswick, N. J. —p. 1001.
Expenditures in Certain Cities for Selected Health Services. Report of Subcommittee on Current Practices of Health Departments of the Committee on Administrative Practice.—p. 1008.
Future of Maritime Quarantine in Canada. J. J. Heagerty, Ottawa, Ont.—p. 1014.
Report of Committee on Transportation. W. L. Bierring, Des Moines, Iowa.—p. 1019.
Newer Aspects of Amebic Dysentery. Report of Subcommittee on Research and Standards.—p. 1023.

Archives of Dermatology and Syphilology, Chicago

34: 555-754 (Oct.) 1936

The American Dermatological Association: Obligations and Objectives. C. G. Lane, Boston.—p. 555.
Pruritus and Hyperesthesia Caused by Partial Sensory Denervation: Experimental Alopecia—Contribution to Study of Alopecia Areata. E. A. Aubrun, Buenos Aires, Argentina, South America.—p. 564.
Certain Phases of Sulfur Metabolism of Skin. J. V. Klauder and H. Brown, Philadelphia.—p. 568.
Tryparsamide: Further Questioning of Alleged Nonspirocheticidal Properties of Pentavalent Arsenical in Treatment of Human Syphilis, with Suggestion Regarding Its Readoption into Curriculum of Therapy for Early Syphilis. H. S. Campbell, Los Angeles.—p. 582.
Halo Nevus: Leukoderma Centrifugum Acquisitum (Sutton): Leukopigmentary Nevus. S. Feldman and I. M. Lashinsky, New York.—p. 590.
Purpura Annularis Telangiectodes: Report of Case. S. C. Way, San Francisco.—p. 605.
*Etiology, Pathology and Treatment of Leukoplakia Buccalis: Report of 316 Cases. F. P. McCarthy, Boston.—p. 612.
Keratoderma and Melanoderma Accompanying Therapy with Gold Compound: Report of Case. S. Irgang, New York.—p. 624.
Fusospirillary Gangrenous Stomatitis. E. B. Tauber and L. Goldman, Cincinnati.—p. 630.
Pemphigus Vulgaris of Erythema Multiforme Variety. O. L. Levin, J. A. Tolmach and J. Schweig, New York.—p. 635.
Failure to Demonstrate Spirochaeta Pallida in Cerebrospinal Fluid of Syphilitic Chinese Patients. L. Pearce, C. K. Hu and J. W. Mu, Peiping, China.—p. 639.
Evaluation of Phytopharmacologic Test of Pels and Macht: Further Report. L. Hollander and R. J. Greb, Pittsburgh.—p. 650.
*Xeroderma Pigmentosum: Inherited Disease Due to Recessive Determiners. Madge Thurlow Macklin, London, Ont.—p. 656.
Exfoliative Dermatitis: Report of Case with Autopsy. T. Butterworth, Reading, Pa.—p. 676.

Leukoplakia Buccalis.—After studying 316 cases of leukoplakia, McCarthy is convinced that in a high percentage of cases extensive involvement of the tongue is definitely related to syphilis but that there is no evidence to indicate a relation between the greater number of instances of leukoplakia observed elsewhere in the oral cavity and syphilitic infection. The predisposing factor in leukoplakia of the tongue is atrophic glossitis of syphilitic origin, occurring in untreated or inadequately treated patients with syphilis of long standing. This type of glossitis, with the secondary sheen of hyperkeratotic leukoplakia, presents a picture almost pathognomonic of syphilis. A characteristic picture of leukoplakia of the tongue is smooth red atrophic areas interspersed with more or less generalized leukoplakic lesions. Frequently the tongue is involved in a sclerotic process with secondary lobulation. The same surface leukokeratotic process is usually associated with this type of glossitis. In contrast to the picture presented by syphilitic glossitis is that of the reaction of the normal tongue in heavy smokers, in whom the hypertrophy and leukoplakia are confined to the papillae, producing a thick, roughened, whitish surface. Constitutional factors have been suggested as important in predisposing a person to leukoplakia or in actually causing it. A lack of vitamin A may result in atrophy of the lingual papillae and predispose the patient to lingual leukoplakia. A hereditary predisposition to degeneration or atrophy of tissue, allied to so-called cancer susceptibility, may be a factor. Leukoplakia is overwhelmingly prevalent in men. This disparity between the sexes may change in the course of time, since women have taken up the use of tobacco. The course of the disease depends entirely on the cause and on preventive and local treatment. Except for the preventive form of treatment, the removal of the irritating factor in the mouth and abstinence from the use of tobacco, the treatment of leukoplakia is unsatisfactory. When the use of tobacco is an etiologic factor and the patient continues to use it, the removal of the leukoplakic lesion is usually followed by a recurrence. The author confines treatment to the use of electrodesiccation and electrocoagulation by monopolar and bipolar high frequency current. The use of radium in the treatment of leukoplakia of the tongue associated with atrophic syphilitic glossitis is provocative of a malignant growth when the treatment is given in small doses over a long time. The use of locally applied irritating or caustic remedies is contraindicated, as there is a possibility of stimulating malignant change in the lesion. The surgical removal of the malignant lesion is indicated in some cases, but in cases of leukoplakia involving the tongue this procedure is often carried to a more radical degree than necessary and the electric current is preferable.

Xeroderma Pigmentosum.—Macklin declares that, contrary to statements made in textbooks of dermatology, xeroderma pigmentosum is found to be inherited, the determiners for which are passed on in the germ plasm from parent to child. It is transmitted as a recessive condition. Consanguineous marriages are found far more frequently among parents of patients with xeroderma pigmentosum than among the general population, the minimal incidence being 21.2 per cent in the series collected. The two sexes are affected equally. Because of the average small size of families, there are more families with one child affected than those with more than one. This does not preclude the possibility or even probability that in any family a second child may be affected. The disease affects males and females equally and may affect both sexes in one family.

Arch. of Physical Therapy, X-Ray, Radium, Chicago

17: 545-608 (Sept.) 1936

Electricity and Medicine. W. Bierman, New York.—p. 551.
Physical Agents in Treatment of Circulatory Diseases of Extremities. N. W. Barker, Rochester, Minn.—p. 554.
Physical Therapy and Management of Stiff Joints. M. S. Henderson, Rochester, Minn.—p. 562.
Pathologic Aspects of Arthritis. R. K. Ghormley, Rochester, Minn.—p. 567.
Atrophic and Hypertrophic Arthritis and Fibrositis. C. H. Slocumb, Rochester, Minn.—p. 571.
*Gastroscopy: Indications, Contraindications, Technic. C. W. Symonds, Pasadena, Calif.—p. 574.
The Sixth International Medical Congress on Physical Medicine. R. Kovács, New York.—p. 581.
Wavelength and Therapeutic Effect. H. F. Wolf, New York.—p. 583.
Study of Colonic Roentgenograms. C. J. Drueck, Chicago.—p. 586.

Gastroscopy.—The extrinsic contraindications to gastroscopy that Symonds lists are aortic aneurysm, enlarged thymus or other tumor and diseases of the spine interfering with mobility, and the intrinsic ones are advanced organic disease, extensive varicosities and acute esophagitis (corrosive and necrotic). Gastroscopy is indicated in every case of persistent or unexplained symptoms referable to the stomach. The indications of special interest are acute and chronic gastritis (chronic, without or associated with additional pathologic processes), gastric symptoms with negative roentgenograms, gastric neurosis, unexplained gastro-intestinal hemorrhage, peptic ulcer, differential diagnosis between ulcer and cancer and neoplasms. Many cases with gastric symptoms with negative roentgen observations and so-called gastric neurosis may be proved by gastroscopy to be gastritis. In the performance of gastroscopy the patient should be in a relaxed state. This is best obtained by the following procedure: 1. Two hours before operation, one capsule of phenobarbital sodium or sodium amytal is administered. 2. One hour before, one-fourth grain (0.016 Gm.) of morphine and a second capsule of phenobarbital sodium or sodium amytal are given. 3. One-half hour before, 1 cc. of a 2 per cent solution of butyn is instilled into the pharynx with a curved cannula. This is swallowed, causing a slight algesia. 4. Fifteen minutes before, the lateral wall of the pharynx is swabbed on both sides with a 10 per cent solution of cocaine by holding the swab against the lateral wall for ten or fifteen seconds on each side in the region of the recurrent laryngeal nerve. This application should be made three times at intervals of five minutes. As the position of the patient is changed with the advancing of the instrument, each must be controlled by a trained assistant to synchronize with the operator's movements of the instrument. Several times during the introduction it may be necessary to aspirate fluid, as the field must be kept clean. As soon as the gastroscope enters the stomach, the light carrier is removed and the lens system with light for illuminating the stomach is put into place. This fits air tight, permitting the stomach to be inflated, which should be done carefully under guidance of the operator's eye. No more air should be introduced than is required to push the stomach away from the window and obtain a clear view. An occasional bulbful or two of air will keep the mucous membrane under clear observation. A good method to prevent overinflation is to have an assistant place a hand over the epigastrium. The whole procedure of introduction and inspection should be completed in from ten to fifteen minutes. While there is some discomfort due to the position of the patient, with proper skill and experience it should not be a painful procedure, and this assurance will do much to enlist the patient's confidence.

California and Western Medicine, San Francisco

45: 217-304 (Sept.) 1936

Better Obstetrics. H. A. Stephenson, San Francisco.—p. 224.
Dermatology: Some Thoughts on Its Future. W. H. Goeckerman, Los Angeles.—p. 227.
Apraxia. S. D. Ingham, Los Angeles.—p. 229.
*Cardiovascular Syphilis: Its Treatment. W. W. Newman, San Francisco.—p. 234.
Bilateral Dislocations of Cervical Spine. R. Soto-Hall and K. O. Haldeman, San Francisco.—p. 238.
Pyodermatoses. N. P. Anderson and S. Ayres Jr., Los Angeles.—p. 243.
Cancer of Thyroid Gland: Report of Ten Cases. F. B. Settle, Long Beach.—p. 247.
Amputation of Thigh: New Amputation in Distal Portion of Lower Third of Thigh. C. L. Callander, San Francisco.—p. 252.
Pathologic Findings at Pars Cardia of Stomach. J. Abowitz, Los Angeles.—p. 255.
Treatment of Exophthalmic Goiter. H. R. Magee, Los Angeles.—p. 257.
Athletic Injuries. P. Thurber, Los Angeles.—p. 261.
Mortality Lessons in Series of 4,029 Gynecologic Operations. H. K. Marshall and R. H. Thompson, Glendale.—p. 263.
Cardiospasm: Successfully Treated by Hydrostatic Dilatation. G. W. Nagel, San Francisco.—p. 271.

Cardiovascular Syphilis.—The incidence of syphilis in 1,000 consecutive ambulatory patients whom Newman has seen in the private practice of cardiology was 3.4 per cent, and of cardiovascular syphilis 3.2 per cent. Of these 43.6 per cent had simple aortitis, 34.4 per cent aortic insufficiency and 22 per cent aneurysm. The blood Wassermann or Kahn reaction was positive in 87.5 per cent and negative in 12.5 per cent. For practical purposes a diagnosis of cardiovascular syphilis is justifiable in any patient with a saccular aortic aneurysm or in any patient more than 40 years of age with aortic insufficiency and a positive Wassermann reaction, provided there is no stenosis of any valve or definite history of rheumatic fever; or in any patient with a positive Wassermann or Kahn reaction, especially if he is less than 50 years of age and complains of substernal pain or dyspnea on exertion, in whom the roentgenogram shows an aortic shadow wider than one would expect for his age or blood pressure, or who has a localized dilatation of the ascending aorta, often best seen fluoroscopically in the left anterior oblique position. Adequate treatment of early syphilis is extremely effective in the prevention of clinical cardiovascular syphilis. In the presence of established cardiovascular syphilis the preponderance of evidence (although not strictly applicable to statistical analysis) is in favor of the beneficial effect of specific therapy, not only with the heavy metals and iodide but also with arsenicals in suitable dosage. The earlier in the course of the disease antisyphilitic therapy is begun, particularly before the onset of aneurysm or aortic insufficiency, the better are the chances of improvement.

Journal of Bacteriology, Baltimore

32: 243-360 (Sept.) 1936

*Spread of Tularemia Through Water, as New Factor in Its Epidemiology. S. P. Karpoff and N. I. Antonoff, Tomsk, Siberia.—p. 243.
Occurrence of Salmonella, Oranienburg Type, in an Infection of Quail. P. R. Edwards, Lexington, Ky.—p. 259.
Studies of Freshwater Bacteria: III. Quantitative Aspects of Direct Microscopic Method. A. T. Henrici, Minneapolis.—p. 265.
Action of Hexamethylenetetramine on Members of Colon and Aerogenes Groups. C. F. Poe and J. H. Williamson, Boulder, Colo.—p. 281.
Atypical Meningococcus Isolated from Cerebrospinal Fluid in the Calcutta Meningitis Epidemic of 1934-1935. Benode Behari Sen, Calcutta, India.—p. 293.
Influence of Optical Activity on Utilization of Tryptophane for Growth by Diphtheria Bacillus. L. C. Bauguess, Iowa City.—p. 299.
Fermentation Reactions of Erysipelothrix Rhusiopathiae. A. W. Deem and C. L. Williams, Columbus, Ohio.—p. 303.
Estimation of Bacterial Populations with Aid of Photoelectric Densitometer. L. G. Longsworth, New York.—p. 307.
Study of Characteristics of Variants Derived from Single Cells of Escherichia Coli. J. C. Torrey and Elizabeth Montu, New York.—p. 329.

Spread of Tularemia Through Water.—Having studied an outbreak of tularemia in 1935, Karpoff and Antonoff were able to prove by exhaustive evidence that water was the mode of spread of the disease. An epidemic broke out among people who were occupied in haymowing. In a week's time nearly all the workers had been taken ill, with the exception of one group of mowers who worked on a plot near by. The disease appeared in from two to eight days after the people came to the meadow lands. In the meadows on which the epidemic broke out there are four eminences, divided by valleys, through which flow a river and three brooks. One group of mowers used the water of the river for drinking and in this group there did not occur a single case of illness; the other mowers, among whom the illness rate attained 100 per cent, used the water of one of the brooks, which at the time in question was running freely. Questioning of the patients showed that near the brook out of which they took their drinking water, they had seen, as they said, some water rats and had killed one of them, but all the people who had been in the fields declared these to be but isolated examples. Besides the rats a few field mice had been observed. In experiments in which the rôle of water in spreading the infection was tested, 100 per cent of the guinea-pigs infected with the water died and their organs showed characteristic pathologic-anatomic changes. From the organs of all these guinea-pigs, cultures of Bacterium tularense were obtained. The cultures that were isolated from water did not differ with regard to virulence from those that were isolated from the suppurated lymph glands of the patients. When these cultures were tested on guinea-pigs, death followed in 100 per cent of cases and the organs showed changes characteristic of tularemic infection. In the outbreak in question the ports of entry were the tonsils, the mouth, the mucosa and the conjunctiva. The anginal form was predominating and the typhoid form came next, while a number of patients showed the glandular-ocular form of illness.

Journal of Lab. and Clinical Medicine, St. Louis

22: 1-112 (Oct.) 1936

Clinical Approach to Rheumatic Patient. R. L. Haden, Cleveland.—p. 1.
Differential Diagnosis of Arthritis from Standpoint of Pathology. E. P. Jordan, Chicago.—p. 6.
British Activities for Control of Rheumatism. Horder, London, England.—p. 12.
Essential Features in Differential Diagnosis of Rheumatoid and Osteo-Arthritis. R. H. Boots, New York.—p. 14.
Differential Diagnosis Between Strümpell-Marie Disease and Osteo-Arthritis of Spine. J. L. Miller, Chicago.—p. 19.
Differential Diagnosis of Acute Rheumatic Fever. R. A. Kinsella, St. Louis.—p. 26.
Differential Diagnosis of Traumatic Arthritis. W. C. Campbell, Memphis, Tenn.—p. 30.
Differential Diagnosis of Tuberculosis Arthritis. F. D. Dickson, Kansas City, Mo.—p. 35.
Differential Diagnosis of Gonococcic Arthritis. S. L. Warren, Rochester, N. Y.—p. 44.
Diagnosis of Gout and Gouty Arthritis. P. S. Hench, Rochester, Minn.—p. 48.
Differential Diagnosis of Periarticular Fibrositis and Arthritis. C. H. Slocumb, Rochester, Minn.—p. 56.
Differential Diagnostic Points of Constitutional Conditions Mistaken for Arthritis Which Produce Skeletal Aches and Pains (Arthralgias, Neuritis, Rheumatism). W. J. Kerr, San Francisco.—p. 64.
Thermocouples for Medical Laboratory: Guiding Principles and Methods of Constructing Apparatus for Surface Cavity, and Intramural Thermometry. P. C. Foster, New Orleans.—p. 68.
*Rapid Flocculation Method for Diagnosis of Syphilis: Technic for Spinal Fluid. F. Rytz, Minneapolis.—p. 82.
Simple and Inexpensive Device for Filling Culture Tubes and Bottles. E. G. Hastings, Madison, Wis.—p. 84.
Examination of Mouse Ovaries in Aschheim-Zondek Test Followed by Castration for Quantitative Testing of Estrogenic Substances. A. I. Weisman and Rosalind L. Moses, New York.—p. 86.
Complete Postmortem Examinations Through Surgical Wounds. S. H. Polayes, Brooklyn.—p. 87.
Quantitative Estimation of Protein by Rapid Method of Kerridge. T. Findley Jr., St. Louis.—p. 89.
New Instrument for Determination of Venous Pressure by Direct Method. L. Cohen, Brooklyn.—p. 94.
Hinton Test for Syphilis: Second Study of Its Clinical Value in 3,000 Patients. L. Hollander, Clara R. Schlesinger and C. L. Schmitt, Pittsburgh.—p. 97.

Rapid Flocculation Method for Diagnosis of Syphilis.—Since the committee appointed by the United States Public Health Service, on the evaluation of serodiagnostic tests for syphilis in the United States, concluded its first report in 1935, Rytz has modified the rapid flocculation method, as first applied to spinal fluid (original abstracted in THE JOURNAL, May 25, 1935, p. 1937). The modified technic renders the test for spinal fluid more sensitive. A strongly positive reaction consists of large, irregular flocculate particles in a crystal-clear fluid. A weakly positive test shows smaller flocculate particles in a slightly hazy fluid. The negative reactions show a hazy fluid with unflocculated emulsion particles. He has compared 185 reactions by this method with the Wassermann test as

carried out in his laboratory. This flocculation method showed fifty-nine positive reactions against thirty-six positive Wassermann tests on the same samples. Of the fifty-nine positive cases by the flocculation method, forty-seven showed positive blood tests, and eight patients with negative blood tests had a definite syphilitic history. Two patients with some symptoms of neurosyphilis remain, at this time, unverified by clinicians.

Journal of Nervous and Mental Disease, New York

84: 373-496 (Oct.) 1936

First Fifty Years of the Philadelphia Neurological Society. W. G. Spiller, Philadelphia.—p. 373.

Three Cases of Mind Blindness (Visual Agnosia): One Due to Softening in Occipital Lobes (Autopsy), One Due to Anterior Poliomyelitis (Nonfatal), One Due to Drugs (Transient). J. M. Nielsen and K. O. Von Hagen, Los Angeles.—p. 386.

*Brain Trauma: II. Residual Lesions in the Brain in Cases of Old Head Injury. N. W. Winkelman, Philadelphia, and J. L. Eckel, Buffalo.—p. 399.

Psychogenic Factors in Polyuria of Schizophrenia. W. R. Miller, Worcester, Mass.—p. 418.

Hoffmann Sign: Its Incidence in University Students. D. H. Echols, Ann Arbor, Mich.—p. 427.

Brain Trauma.—Winkelman and Eckel studied five cases of the posttraumatic state for a period of from four months to four years. Clinically the patients showed personality change and convulsive seizures as the most common manifestations. Focalizing signs and symptoms were present in only one case. Activation of a preexisting syphilitic process resulted in the formation of a gumma at the point of trauma. Histopathologically the patients showed focal lesions of hemorrhage and softening, with scattered petechial lesions of the same sort. The changes in the brain in general were to be attributed to the original concussion with the secondary changes due to anoxemia from increased intracranial pressure. These involved the ganglion cells and blood vessels in addition to a universal glial overgrowth. Adhesions of the pia-arachnoid to the cortex and to the dura were present in nearly all the cases. In one case an abscess developed at the point of impact in a patient with an old middle ear disease, with generalized convulsions occurring seven days after injury, although intracranial pressure signs did not occur until three years later.

Journal of Pediatrics, St. Louis

9: 279-416 (Sept.) 1936

*Mediterranean Disease—Thalassemia (Erythroblastic Anemia of Cooley): Associated Pigment Abnormalities Simulating Hemochromatosis. G. H. Whipple and W. L. Bradford, Rochester, N. Y.—p. 279.

Observations on Morphology of Erythrocytes in Mediterranean Disease—Thalassemia (Erythroblastic Anemia of Cooley). W. L. Bradford and Jane Dye, Rochester, N. Y.—p. 312.

Intravascular Clotting in Abandoned Fetal Channels in the New-Born. W. A. Mulherin and J. Krafka Jr., Augusta, Ga.—p. 318.

Outline of the Pediatrist's Relation to Mental Hygiene. C. A. Aldrich, Winnetka, Ill., and B. S. Veeder, St. Louis.—p. 323.

*Presence of Meningococcus in Nasopharynx of Normal Individuals, and Bactericidal Property of Blood Against Meningococcus. N. Silverthorne, Toronto.—p. 328.

Mediastinal Lymphosarcomas in Childhood. F. W. Wiglesworth, A. E. Childe and A. Goldbloom, Montreal.—p. 331.

Evolution of Adult Type of Tuberculosis from the Childhood Type: Evidence in Favor of Endogenous Reinfection: Preliminary Report. J. A. Johnston, Detroit.—p. 350.

Study of Comparative Value of Cod Liver Oil, Viosterol and Vitamin D Milks in Prevention of Rickets and of Certain Basic Factors Influencing Their Efficacy. Martha M. Eliot and E. M. Nelson, Washington, D. C.; D. J. Barnes and Florence A. Browne, Detroit, and Rachel M. Jenss, Washington, D. C.—p. 355.

Mediterranean Disease—Thalassemia.—Four years ago, Whipple and Bradford reported the clinical and necropsy features in a typical case of Mediterranean disease. As the pigment abnormalities there described had not been noted in other published reports, they could not stress their importance. They now report three more cases with complete necropsy reports. They have had opportunity to study certain organ tissues from two other cases. All this material gives them reasonable security in their belief that the pigment deposits are just as characteristic of this disease complex as are any other factors. The disease presents a uniform clinical picture consisting of a progressive anemia beginning usually during the first two years of life and terminating in death in most instances before adolescence. The blood picture, though not distinctive, is uniform and is characterized by marked irregularity in the size and shape of the red cell, fragmentation and erythroblastosis. All stages of erythropoiesis may be seen in the peripheral blood. The hemoglobin distribution within the matured red cell may be very irregular. After splenectomy, showers of nucleated red cells always occur. Definite retardation of growth results. As the disease progresses, the typical mongoloid features develop, probably because of bone changes. Enlargement of the spleen is proportionally greater than that of the liver, but, when the former is removed, the latter seems to increase in size. To this group of clinical features the addition of the abnormalities that occur in the bones, the unusual pigment disturbances, and the racial and familial distribution complete a characteristic syndrome. Therefore the disease is due to some racial, inherited defect which is responsible for the abnormalities of the hematopoietic tissues (of the order of pernicious anemia), the bone changes (of the order of acromegaly) and the pigment abnormalities (virtually identical with hemochromatosis). This suggests a deficiency state that may be remediable when completely understood and gives adequate grounds for a variety of therapeutic tests. The anemia may be classified as microcytic and hypochromic. The following therapeutic measures failed to modify the clinical picture: blood transfusions, plasma and cell extracts, primary or secondary anemia liver extracts, fetal liver extract, spleen extract, raw pancreas, adrenal cortex extract, estrogenic substance, vitamin B_1 concentrate, iron and copper.

Meningococcus Carriers.—Silverthorne investigated the carrier rate in a noncontact population and the bactericidal property of the blood of normal persons and of noncontact carriers against various strains of meningococci. A total of 1,227 swabs were taken monthly from sixty-three normal healthy adults over a period of two years; 19.8 per cent of these were positive for the meningococcus. On these monthly examinations the number of positive individuals varied from 16 to 28 per cent. No less than 41 per cent of the group of sixty-three were positive at one time or another during the period of study; eleven were persistent, thirteen intermittent and two transient carriers. Eleven noncontact carrier strains were examined by the bactericidal and mouse-mucin tests; three of these strains were found to be virulent and eight were found to be avirulent. Carriers of the meningococcus possess bactericidal power in their blood to their respective strains, whether these strains are virulent or avirulent. Also, samples of blood from carriers possess bactericidal power to certain virulent cerebrospinal fluid strains. The determination of the virulence of strains of meningococci by means of the mouse-mucin and bactericidal tests may serve as a useful means of selecting strains for the preparation of therapeutic serum.

Laryngoscope, St. Louis

46: 647-730 (Sept.) 1936

Fluoroscopic Bouginage of Stricture of Esophagus. H. P. Mosher, Boston.—p. 647.

Recurrent Lipoma-Myxochondroma-Fibroma of Larynx: Case Exhibiting Unique Features. A. Palmer and L. Mehler, New York.—p. 653.

Scopulariopsis in Otomycosis. M. E. Pinkerton and E. L. MacQuiddy, Omaha.—p. 670.

Interesting Cases of Lateral Sinus Thrombosis. H. M. Scheer, New York.—p. 674.

Hemolytic Streptococcic Meningitis with Recovery. G. H. Poirier and B. E. Lovesey, Boston.—p. 680.

Ear Drumhead Model. G. W. McAuliffe, New York.—p. 686.

Incidence of Sinusitis and Nasal Polyps in Bronchial Asthma. S. F. Kelley, New York.—p. 692.

Interlobar Abscess Probed and Drained Through Cribriform Plate: Cure of Asthma. I. Dowling, Albany.—p. 699.

*Effect of Intranasal Phenol Application in Hay Fever: Quantitatively Studied by New Intranasal Swab Test with Pollen Extracts. F. Vistreich, New York.—p. 717.

Intranasal Phenol Application in Hay Fever.—Vistreich observed the effect of intranasal phenol application in twenty-eight consecutive cases of early and late hay fever. The treatment is not followed by stormy reaction or long convalescence. From 90 to 100 per cent relief was obtained in 75 per cent of the cases, from 75 to 90 per cent relief in 8.3 per cent, from 50 to 75 per cent relief in 12.5 per cent and no relief in 4.2 per cent. By intranasal swab tests with serial dilutions of pollen extracts it was proved that this treatment produces an actual decrease in the sensitivity of the nasal mucosa to pollen. By periodic testing it has been found that this state of relative insensitiveness is not permanent. Its average duration in the present group of cases was approximately from seven to eight weeks.

Maine Medical Journal, Portland

27: 175-194 (Sept.) 1936

Recent Advances in Gastro-Intestinal Surgery. W. V. Cox, Lewiston.—p. 175.
*Electrosurgical Treatment of Cervical Lacerations, Erosions and Endocervicitis. R. L. Barrett, New York.—p. 178.
Tumors: Definition and Classification. J. Gottlieb, Lewiston.—p. 184.

27: 195-212 (Oct.) 1936

Carcinoma of Breast. C. M. Robinson, Portland.—p. 195.
Carcinoma of Uterus. M. F. Ridlon, Bangor.—p. 198.
Cancer of Gastro-Intestinal Tract. E. H. Risley, Waterville.—p. 200.
Pathology of Carcinoma of Breast, Pelvis and Gastro-Intestinal Tract. A. H. Morrell, Augusta.—p. 205.
Appendicitis and the Schilling Count. R. A. Beliveau, Lewiston.—p. 207.

Electrosurgical Treatment of Cervical Lacerations.—Barrett finds that electrosurgical diathermy with the Hyams technic, the Cherry Ende technic or the simple ball coagulation technic is suitable for the treatment of the majority of the cervical lacerations, erosions and endocervicitis. The method is not free from danger. Too extensive destruction of tissue may lead to primary or secondary hemorrhages. Deep destruction of tissue high in the cervical canal, especially if there has been carbonization, tends to heal with excess fibrous tissue with its consequent impairment of drainage, stenosis, sterility and dystocia. Curtis has shown that stenosis and cavitation in the upper cervix with secondary infection and lack of drainage is a frequent cause of irritant leukorrhea, epithelial metaplasia and leukoplakia. A thorough dilation of the cervix is indicated if the treatment is to be carried above the level of the lower third of the canal. The dilation should be repeated after healing occurs if there is any sign of constriction. Carbonization and deep destruction of tissue should be avoided. Electrosurgical diathermy is contraindicated in the presence of an active or latent pelvic infection.

New England Journal of Medicine, Boston

215: 517-568 (Sept. 17) 1936

Principles of Therapy in Patients with Congestive Heart Failure. T. R. Harrison, Nashville, Tenn.—p. 517.
*Cancer of the Breast: End Results, Massachusetts General Hospital, 1927, 1928 and 1929. C. C. Simmons, G. W. Taylor and H. D. Adams, Boston.—p. 521.
Address to the Staff of the Worcester City Hospital, May 1936. S. B. Woodward, Worcester, Mass.—p. 526.
Artificial Pneumothorax in Treatment of Tuberculosis. J. D. Spring, Nashua, N. H.—p. 530.
Sexual Sterilization in New Hamsphire. S. Stone, Concord, N. H.—p. 536.
Progress in Laryngology. L. A. Schall, J. R. Richardson and W. Mueller, Boston.—p. 546.

215: 569-604 (Sept. 24) 1936

Efficacy of Medical Treatment in Essential Hypertension. R. S. Palmer, Boston.—p. 569.
Nonspecific Urethritis: Its Causes, Differential Diagnosis, Examination Routine and Treatment. N. D. Shaw and W. M. Burnet, Chicago.—p. 572.
Ruptured Ovarian Cyst in Childhood: Report of Case. G. C. King and C. H. Hawes, Fall River, Mass.—p. 576.
Legal Aspects of Industrial Dermatoses. J. G. Downing, Boston.—p. 577.
My Personal Experience with Extramural Service. F. C. Phelps, Vergennes, Vt.—p. 580.

Cancer of the Breast.—Simmons and his co-workers report the five year end results of 159 cases of cancer of the breast treated by radical operation at the Massachusetts General Hospital during the three years 1927, 1928 and 1929. There were 43.4 per cent of five year cures following radical operation. Of the fifty-eight persons in whom the disease was limited to the breast, forty-four were living without evidence of recurrence from five to seven years after operation. Of the 101 patients in whom the axillary glands were involved, twenty-five were living without evidence of disease from five to seven years after operation. The prognosis was found to depend more on the extent of the disease and the pathologic index of the malignant condition of the tumor than on any other factors. This coincides with the observations in the former groups studied. The median duration of the disease before operation of the cases without axillary involvement was three months. The median duration with axillary involvement was six months. The importance of early diagnosis and treatment is shown by comparing results of operation in these two groups. Preoperative roentgen treatment was given to a certain number of these patients. It had no effect on the results when the cases were placed in comparable groups. The dosage was much less than that advocated at the present time but was similar to that given at other institutions during the period under investigation.

Public Health Reports, Washington, D. C.

51: 1327-1362 (Sept. 25) 1936

Acute Response of Guinea-Pigs to Vapors of Some New Commercial Organic Compounds: XIII. Methyl Formate. H. H. Schrenk, W. P. Yant, J. Chornyak and F. A. Patty.—p. 1329.

Radiology, Syracuse, N. Y.

27: 261-390 (Sept.) 1936

Primary Bone Tumors in Children. L. S. Goin and R. L. Carroll, Los Angeles.—p. 261.
*Asbestosis: Roentgenologic Review of Seventy-One Cases. J. R. Shull, Charlotte, N. C.—p. 279.
Influence of Wavelength on Depth Dose as Measured by Physical and Biologic Means. P. S. Henshaw and D. S. Francis, New York.—p. 293.
Acute Gastric Dilatation of Stomach During Attack of Migraine. J. Kaufman and I. Levine, Brooklyn.—p. 301.
Some Lawsuits I Have Met and Some of the Lessons to Be Learned from Them (Tenth Instalment). I. S. Trostler, Chicago.—p. 303.
Radiation Therapy in Cancer of Cervix. L. C. Kress and M. C. Reinhard, Buffalo.—p. 318.
Syphilis of Esophagus. P. S. Avery, New Brunswick, N. J.—p. 323.
Radioresistant Ewing Sarcomas of Bone. A. Brunschwig, Chicago.—p. 328.
Small Intestine: Inflammatory Lesions and Accompanying Reactions. L. G. Cole and R. E. Pound, New York.—p. 330.
X-Ray Diffraction Studies of Tendon and Intestinal Wall Collagen. G. L. Clark and J. A. Schaad, Urbana, Ill.—p. 339.
Typhoid Spine. A. Bowen and C. L. McGehee, Fort Sam Houston, Texas.—p. 357.
Significance of X-Ray Control in Artificial Fixation of Mediastinum Supplementing Closed Intrapleural Pneumonolysis in Cavernous Pulmonary Tuberculosis. F. Baum, Newark, N. J.—p. 359.
Improved Method for Making Reproductions from X-Ray Films. B. H. Nichols and J. C. Root, Cleveland.—p. 362.

Asbestosis.—Shull defines asbestosis as a disease of the lungs caused by the inhalation of asbestos dust and fiber. It is classified as a pneumoconiosis and is characterized roentgenologically by an early interstitial fibrosis with progression into a terminal diffuse fibrosis. As the disease progresses there develops a filmy, hazy appearance of the lung, which has been aptly described as a "ground-glass appearance." The right side of the heart is frequently enlarged in the moderately advanced cases, and it is a common observation in the markedly advanced cases. Another finding characteristic of this disease is the presence of peculiar golden colored, crustation-like bodies in the lungs of these patients. Clinically, the most striking symptom is undoubtedly dyspnea. During the latter part of 1934 the author examined the chests of seventy-one of 100 workers who had been dismissed from local asbestos plants. All had undergone physical examination before they were referred for roentgenologic study and were found to be physically disabled. The average age was 34.4 years and the time of exposure varied from sixteen months to twenty-one years. In eight recognized cases of tuberculosis (11.3 per cent) in the entire series the degree of infiltration was only slight to moderately advanced and one or both upper lobes were involved. Only two cases appeared active. Since these examinations were made, five patients have died. Of the remaining sixty-six patients, twenty-one have been reexamined recently. In studying the original and follow-up roentgenograms of the series and contrasting them with a number of plates of other types of pneumoconiosis, it has been possible to make certain observations which seem to be peculiar to this group of asbestosis cases as a whole. Furthermore, it was obvious that a classification could be effected. Since the one constant feature of all these cases is unquestionably the diffuse fibrosis, this sign was taken as the "yard stick" in compiling such a classification (slightly, moderately and markedly advanced cases). Of sixteen slightly, thirty-five moderately and twenty markedly advanced cases, 37.5, 62.8 and 95 per cent respectively showed a right-sided hypertrophy, 0, 28.6 and 45 per cent pericardial and pleural thickening, 12.5, 48.6 and 80 per cent a high left diaphragm and 6.3, 65.7 and 95 per cent an emphysematous type of chest.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Medical Journal, London

2: 573-610 (Sept. 19) 1936

Anemia of Pregnancy. W. C. Smallwood.—p. 573.
*Hypochromic Anemias of Pregnancy and Puerperium. H. W. Fullerton. —p. 577.
Preventive Measures in Dermatology. R. M. B. MacKenna.—p. 581.
*Cervical Gland Tuberculosis: Case Against Surgery. B. C. Thompson. —p. 584.
Homework. W. Brockbank.—p. 587.

Hypochromic Anemias of Pregnancy.—Fullerton found that the average hemoglobin levels of poor women fell during pregnancy up to the thirty-seventh week of gestation and then rose slightly before delivery. A rise in the hemoglobin level occurred from forty-eight hours post partum to from six to eleven months after delivery. Even in women of the poor classes the transference of iron from the mother to the uterus and its contents is compensated wholly or to a large extent by dietary iron. In cases in which this demand exceeds the retention of dietary iron, the degree of maternal iron deficiency which results is only slight. When hypochromic anemia in pregnancy is marked, anemia has probably existed before the pregnancy but has been made more apparent by physiologic hydremia. Therefore the conception that uncomplicated pregnancy frequently produces a severe degree of hypochromic anemia should be discarded. The blood loss at parturition varies greatly in degree and often produces severe hypochromic anemia.

Cervical Gland Tuberculosis.—Observation of forty-four patients led Thompson to conclude that tuberculosis of the cervical glands is seldom, if ever, completely removed by surgical means, and that so-called radical excision is in practice usually a partial operation. This partial excision can be justified only if proved by results to be superior to other methods of treatment. The high rate of local recurrence and the degree of permanent disfigurement due to cicatrization found in this series of cases indicates the reverse. It is also shown from the figures of other observers that the operation does not prevent the subsequent development of pulmonary tuberculosis. Additional disadvantages are the inconvenience caused to the patient by hospitalization, the frequent necessity for repeated operations, and the risk of paresis from nerve injury. It is held that conservative treatment has none of these disadvantages and ultimately produces results in every way more satisfactory.

Glasgow Medical Journal

8: 121-200 (Sept.) 1936

The Doctor's Back Garden. J. Bridie.—p. 121.
Diagnosis and Treatment of Bone Sarcoma. W. B. Coley.—p. 128.
Dr. William B. Coley: Postscriptum. A. Young.—p. 165.

Irish Journal of Medical Science, Dublin

No. 129: 565-612 (Sept.) 1936

Looking and Seeing (Movements and Fixation of Eyes). G. Holmes.—p. 565.
*Late Ether Convulsions: Derangement of Heat-Regulating Mechanism of Body as Major Factor in Their Causation: Preliminary Note. F. W. G. Smith.—p. 577.
Treatment of Appendicitis. R. A. Stoney.—p. 591.

Late Ether Convulsions.—Smith illustrates the close connection between what are called "ether convulsions" and heat hyperpyrexia. The literature of both subjects indicates that ether convulsions and heat hyperpyrexia are identical. The phenomena of postoperative thyroid crises may be a manifestation of heat effects in a disordered heat regulating mechanism. The treatment adopted for these crises follows closely that of heat hyperpyrexia. Some cases of death from status lymphaticus may have a similar origin. Hadfield remarked (1928) that heat was the sole common factor in all the ether convulsion cases which he summarized. The most important prophylactic measure would be the recognition of the fact, generally, that heat hyperpyrexia can occur in the modern operating room in temperate countries, a sense of proportion being maintained, as the reported cases occur in only 1 in 5,000 administrations. Surgical patients in hot weather periods should be encouraged to drink large quantities of liquids, and their urine should be kept alkaline. There should be a sufficiency of salt in the diet. The rectal temperature and pulse rate of patients for operation should be recorded prominently on their charts. In hot weather the substitution of scopolamine for preoperative atropine should be considered. Potential subjects of heat hyperpyrexia requiring immediate operation should have their knee jerks tested first and be operated on in a cool room; excessive covering of the body by rubber sheetings should be avoided and the head slightly raised if possible. Anesthesia could be induced and maintained with the head resting on an ice bag or an ice bag in close contact with the carotid vessels. Induction with chloroform or a mixture should be considered. The acute case should be diagnosed early by the taking of the rectal temperature and treated on general heat hyperpyrexial lines modified by the circumstances present. Pentobarbital sodium or *n*-methyl-cyclohexenyl methylmalonyl-urea could be given for the convulsions. After-treatment is extremely important, as recurrences of hyperpyrexia are frequent and the cases must be watched carefully for some days.

Medical Journal of Australia, Sydney

2: 251-282 (Aug. 22) 1936

Avenues of Progress in Maternal Welfare. R. M. Allan.—p. 251.
Intraperitoneal Adhesions. L. M. McKillop.—p. 259.
Treatment of Acute Retention of Urine in General Practice. C. Edwards.—p. 260.
Some Notes on "Evipan" and "Evipan Sodium." A. G. Bennett.—p. 266.

South African Medical Journal, Cape Town

10: 565-596 (Aug. 22) 1936

Principles of Treatment of Acute Empyema. F. D. du T. van Zyl.—p. 567.
Eventration of Diaphragm and Its Clinical Aspects. L. I. Braun.—p. 570.
Forensic and Sociological Aspects of Dagga Problem in South Africa. J. M. Watt and Maria G. Breyer-Brandwijk.—p. 573.
Suprasellar Meningioma: Case. D. J. Wood.—p. 580.

Chinese Medical Journal, Peiping

50: 885-1012 (July) 1936

Pulmonary Tuberculosis in Diabetes Mellitus. S.-H. Wang, C.-P. Chang and C. K. Hsieh.—p. 885.
*Cirrhosis of Liver. I. Etiology, Symptomatology, Liver Function Tests and Gastric Juice Findings. C.-F. Wang.—p. 891.
Id.: II. Calcium, Total Proteins, Sugar and Chloride Distribution in Various Body Fluids. C.-F. Wang.—p. 903.
Natural Infection of Phlebotomus Chinensis with Flagellates Morphologically Indistinguishable from Those of Leishmania Donovani. C. J. Sun, Y. T. Yao, H. J. Chu and C. C. Wu.—p. 911.

Cirrhosis of Liver.—In reviewing a series of fifty-four cases of cirrhosis of the liver Wang found that thirty-two of the cases (59.3 per cent) occurred in the fourth and fifth decades of life. The disease occurs largely in the working classes, especially in farmers. Alcohol, syphilis and malaria may be considered etiologic factors in its production. The galactose tolerance test, detection of urobilin in urine and the van den Bergh reaction were valuable for detecting and estimating the amount of liver derangement. Ten of twenty-seven fractional gastric analyses (37 per cent) demonstrated achlorhydria. Nearly all patients had leukopenia and half had anemia. Only five cases (9.2 per cent) showed hematemesis. Symptoms of gastric disorder were present in all but two of the cases; roughly one half of the patients gave a history of gastric disturbance before the onset of ascites. Enlargement of the liver was found in nine cases (16.6 per cent), enlargement of the spleen in eighteen (33.3 per cent) and thirty-four (63 per cent) presented jaundice.

Japanese Journal of Gastroenterology, Kyoto

8: 121-170 (Sept.) 1936

Study on Gastric Movement After Amputation of Vagus Nerves. S. Hattori.—p. 121.
Influence of Blood in Cases of Renal Disturbances on Carbohydrate Metabolism of Liver. Y. Kansai.—p. 136.
Experimental Studies on State of Functional Promotion of Liver (Hyperhepatism). I. Influences of Several Cholagogues on Liver Function. Y. Matsuoka.—p. 145.
Id.: II. Incretory Glands and Hyperhepatism. Y. Matsuoka.—p. 152.
Id.: III. Influence of Lecithin on Liver Function. Y. Matsuoka. —p. 158.
Id.: IV. Influence of l-Asparagic Acid on Liver Function. Y. Matsuoka. —p. 166.

Bull. et Mém. de la Soc. Méd. des Hôpitaux de Paris

52: 1211-1276 (July 20) 1936. Partial Index

Hodgkin's Disease with Eosinophilia and Rapid Evolution. C. Aubertin and A. Pergola.—p. 1214.
Hyperfolliculin Syndrome. Gilbert-Dreyfus, A. Mathivat and A. Wimphen.—p. 1234.
Pathogenesis of Cardiac Epilepsy. Riser, Planques and Petel.—p. 1242.
*Partial Icterus. N. Fiessinger and G. Boudin.—p. 1259.

Partial Icterus.—The type of icterus which is characterized by localization in one segment of the body, most often in the upper portion, is discussed by Fiessinger and Boudin. This localization, when it occurs, is only the consequence of an edematous infiltration of dependent portions. The first patient was a woman with the common type of Laënnec's cirrhosis. When this patient was first observed the icterus was generalized, but, as ascites and edema developed, the location of the icterus became the reverse of that of the edema. This local washing of the icterus could be experimentally reproduced by the authors by the injection of physiologic solution of sodium chloride into the subcutaneous tissue stained with the characteristic icterus color. The interest of this phenomenon of partial icterus seems to be purely symptomatic. The mechanism is simply the washing away of icterus by edematous infiltration of certain regions. This result, however, is aided by the fact that edema is produced at a stage when the bilirubinemia is decreasing and by the simple dilution of the bilirubin by the excess of fluid.

Presse Médicale, Paris

44: 1449-1464 (Sept. 16) 1936

Generalized Peritonitis from Typhoid Intestinal Perforation. A. Mouchet.—p. 1449.
Physiopathogenesis of Lesions in Infectious Diseases, Especially Bacillary Infection. R. Pons.—p. 1451.
*Local Reactions of Capillaries to Histamine and Acetylcholine in Course of Different Varieties of Hypertension. E. Dicker.—p. 1454.

Reactions of Capillaries to Histamine in Hypertension.—Dicker studied the local capillary reactions in different varieties of hypertension under the influence of histamine and acetylcholine. His method of observation differed from that of Ernstene and Snyder only in the fact that he calculated simultaneously in the same person the surface of the erythema produced by the intradermal injection of 0.05 cc. of a 1:1,000 solution of histamine and that produced by the intradermal injection of a drop of a 1:100 solution of acetylcholine. As a result of his studies he concluded that in the normal state the extent of the erythema following the intradermal injection of histamine or acetylcholine attains a mean of 25 and 17 sq. cm. respectively. It varies from one subject to another but in the same person preserves a satisfactory consistency in different examinations. In patients with essential hypertension and arteriosclerotic hypertension the surface area of the erythema produced does not differ from that of normal subjects. In nephritic hypertension, malignant hypertension and malignant nephrosclerosis, the erythema produced by the injection of these substances is slightly increased but the surface area is strongly reduced. In the course of certain infections that may produce acute nephritis, such as scarlet fever and streptococcic tonsillitis, the intensity and area of reaction to histamine and acetylcholine are reduced during the period of resultant hypertension. These facts, the author believes, constitute an important argument in favor of the conception which attributes the development of essential hypertension and malignant hypertension to two distinct mechanisms. The latter is probably associated with a state of constriction of the peripheral vessels.

44: 1465-1480 (Sept. 19) 1936

*Skin Reactions to Tuberculin in Children from Birth to the Age of 2 Years. P. Nobécourt and S. B. Briskas.—p. 1465.
Artificial Production of Thyroid Hyperplasia. H. Zondek.—p. 1469.

Skin Reactions to Tuberculin in Small Children.—Nobécourt and Briskas studied the tuberculin reactions of 6,607 nurslings less than 2 years of age. These tests were performed over a period of fifteen years, from 1921 to 1935 inclusive. Terminal states of anergy were encountered in 8.9 per cent of the tuberculous patients. Furthermore, almost all the cases of tuberculosis in this age group were in an active state. The number of infants infected with tuberculosis was small during the first months but increased with age. The number of patients with active tuberculosis was roughly parallel. During the second year the proportion of infected infants who had had inactive tuberculosis was much greater than during the first year of life. Also during the second year infected girls more often than boys had active tuberculosis. The latter fact may be explained perhaps on the basis of certain predispositions.

Revue Médicale de la Suisse Romande, Lausanne

56: 657-720 (Sept. 25) 1936

*Tuberculous Infection in Children of Country. P. Rochat.—p. 657.
Bilateral Pleuropulmonary Perforation with Necropsy: Case. F. Cardis and A. Gilliard.—p. 669.
Appearance of Autonomous Pocket on Visceral Pleura in Course of Artificial Pneumothorax. J. Stephani, T. Stephani and R. Kirsch.—p. 681.
Technic of True Pleural Endoscopy Before Cauterization of Adhesions. M. O. Mistal.—p. 687.

Tuberculous Infection in Country Children.—In 1935 Rochat studied 450 students by means of the roentgen ray and the Pirquet reaction. The Pirquet test was found negative in 80 per cent of the subjects from 12 to 16 years of age and in 90 per cent of the younger children. These facts have a considerable diagnostic importance not only for the little ones but also for the older children. A year later the children with positive tuberculin tests reacted in an identical fashion. The papule showed the same aspect as in the previous test. Poor hygiene conditions do not constitute the determining factor in the dissemination of tuberculosis. Tuberculosis is a disease of wretched lodgings only if there are also patients with the disease present. Of sixty children with positive reactions there were only ten instances in which the source of the contagion was known. The latter fact suggests the probability that the infection of the children took place most often by carriers of the germs who were in apparent good health.

Clinica Medica Italiana, Milan

67: 583-654 (Sept.) 1936

Intramural Hematoma from Rupture of Abdominal Aorta: Possible Atheromatic and Syphilitic Origin of Aortic Dissecting Aneurysm; Case Report. A. Baccaredda.—p. 585.
Pulmonary Localization of Actinomyces Albus with Generalization: Case. G. Ferrari and P. De Filippi.—p. 611.
*Hydrophilia in Tissues and in Blood in Cholecystitis and Catarrhal Jaundice. E. Poli.—p. 641.

Hydrophilia in Tissues and Blood in Cholecystitis.—Poli calls attention to the relation that exists between liver diseases and disturbances of the water metabolism. The author found that in patients suffering from cholecystitis or from catarrhal jaundice the water is retained by the blood and the tissues. The factors that cause the tendency of blood and tissues to water retention or actual hydrophilia in these patients are stasis of the portal circulation, defective elaboration of bile salts, dysfunction of the liver in controlling the balance of the organic electrolytes (because of a defective chemistry of the bile secretion) and changes in the amount of lipids contained in the blood serum. These factors, which become apparent in the course of cholecystitis and catarrhal jaundice, are capable of disturbing the organic water metabolism.

Policlinico, Rome

43: 1855-1898 (Oct. 19) 1936. Practical Section

*Amenorrhea in Diabetes. R. Bompiani.—p. 1855.
Dermo-Epidermal Grafts: Technic and Results. D. Clemente.—p. 1861.
Hemotherapy. S. Colaneri.—p. 1864.

Amenorrhea in Diabetes.—Bompiani says that amenorrhea and the development of involutive changes of the genitalia in diabetes are secondary to alterations of the anterior lobe of the hypophysis and of the diencephalon. By reviewing clinical and experimental reports in the literature it is obvious that the anterior lobe of the hypophysis and the hypothalamic nuclei are the structures by which the sugar metabolism and the phenomena of the uterine-ovarian cycle are controlled. On the one hand, hypophyseal syndromes are frequently associated with changes in the sexual function and alterations of the genitalia and, on the other, anatomic alterations of the hypophysis and of the diencephalon are often found in diabetes of definite insular origin. According to the author, the hypophyseal-hypothalamic pathogenic mechanism of amenorrhea explains the frequent production of amenorrhea preceding diabetes and the

reestablishment of the uterine-ovarian cycle and the regaining of fecundity in women suffering from amenorrhea and treated with insulin.

Radiologia Medica, Milan

23: 733-836 (Oct.) 1936

*Generalized Osteopathy with Multiple Symmetrical Striae of Reabsorption (Milkman Syndrome). V. Dall'Acqua, P. Levi and L. Bordoli.—p. 733.

Prolonged Roentgen Therapy at High Voltage and Fractional Doses in Relation to Economy in Centers for Treating Cancer. F. Perussia.—p. 750.

Postbronchographic Infiltration of Lung by Iodized Oil: Pneumography Following Bronchography. A. Vallebona.—p. 756.

Importance of Roentgen Study of Lung in Interpreting Modifications of Lung in Course of Retractile Collapse Therapy. A. Biasini.—p. 773.

Generalized Osteopathy with Symmetrical Striae.—The skeletal disease to which Dall'Acqua and his associates refer develops in persons beyond the second decade of life. It is progressive and fails to respond to treatment. The characteristics of the disease are pain in the bones, disturbances in gait and a peculiar multiple symmetrical involvement of the skeleton. The roentgen examination of long and flat bones shows, in several of them, multiple symmetrical transverse bands (pseudofractures) of increased transparency, about 3 or 4 mm. long, which involve the bone superficially or in its entire depth. The pseudofractures do not cause separation and displacement of the fragments. The condition is the result of local reabsorption of the bone. It is different from Looser's zones of decalcification. The bands are located at the epiphysis and the metaphysis rather than at the diaphysis. At the site of the pseudofracture none or only a slight periostic reaction takes place. The pseudofractures occur simultaneously in corresponding bones on the two sides of the skeleton, but the size and exact location of the fractures may be different. During the evolution of the disease the viscera remain normal, as proved by clinical and roentgen examinations. The blood phosphatases are increased. A differential diagnosis is made by the authors between the disease and rickets, osteomalacia, osteogenesis imperfecta and multiple myeloma of the bones. The authors conclude that the disease is rare and probably due to nervous and vascular disturbances. Their case is the third reported in the literature.

Semana Médica, Buenos Aires

43: 961-1032 (Oct. 8) 1936. Partial Index

Hypogastric Iliac Artificial Anus. R. Finochietto.—p. 961.

*Sympathetic Nervous System of Blood Vessels in Thrombo-Angiitis Obliterans. M. Yanovsky.—p. 968.

Examination of Mediastinum: Etiologic Diagnostic Value in Lung Diseases. G. A. Bosco.—p. 991.

Bronchial Asthma from Point of View of Allergy. J. A. Bozzola.—p. 1002.

Double Congenital Abnormality: Roger Disease and Stenosis of Isthmus of Aorta; Case. O. Lombardi.—p. 1004.

Edema from Jaundice Liver Diseases: Case. R. Cernich, J. M. Palazón and J. D. M. de Lellis.—p. 1008.

Thrombo-Angiitis Obliterans.—Yanovsky names thrombo-angiitis obliterans (of Buerger's type) neuro-angiitis obliterans, indicating involvement of the sympathetic nerves and blood vessels in the pathologic process. The condition generally occurs in the blood vessels of the extremities in patients ranging in age from 20 to 35 years with an emotional, psychic and neurovascular predisposition. The early neurovascular lesion consists in inflammation and fibrosis of the adventitia and its sympathetic fibers. Degeneration of the sympathetic fibers and disorganization of the vascular layers from the adventitia to the intima and endothelial alterations follow. The lumen of the blood vessels is occluded by a thrombus (which is secondary to the endothelial changes) or by the propagation of fibrosis from the outer to the inner layers of the vessels. In normal peripheral blood vessels, sympathetic fibers exist only in the adventitia. The presence of sympathetic fibers in the inner layers of the blood vessels in thrombo-angiitis obliterans is due to the inward propagation of the lesion and disorganization of the vascular tissues. Certain nervous oval cells which can be seen at the adventitia of the blood vessels are peripheral cells and not multipolar ganglions. Probably they are concerned in maintaining the tonus of the local vessels. The formation of a thrombus is not specific in thrombo-angiitis obliterans. It may exist in certain vascular diseases with an etiopathogenesis different from that of thrombo-angiitis obliterans. The endocrine glands have a direct action on the sympathetic nerves of the blood vessels. Nervous lesions develop in certain chronic forms of thrombo-angiitis obliterans. Arteriosclerosis is the third stage in the evolution of the disease. It may be followed by calcification of the vascular walls. Typical clinical forms of thrombo-angiitis obliterans are biologically and anatomopathologically different from syphilis. The administration of antisyphilitic treatment does not induce changes in the evolution of the disease. The condition can be easily mistaken because of the fact that the intravasal alterations of chronic syphilitic arteritis are similar to the occlusion in thrombo-angiitis obliterans.

Medizinische Klinik, Berlin

32: 1161-1200 (Aug. 28) 1936. Partial Index

Exostoses of Foot and Their Clinical Significance. O. Dittmar.—p. 1161.

Treatment of Chronic Polyarthritis of Childhood. G. Hohmann.—p. 1163.

*Early Diagnosis of Wandering Epiphysis on Head of Femur During Adolescence. C. Mau.—p. 1166.

Neuropathic Articular Disorders and Their Early Roentgenologic Diagnosis. G. von Pannewitz.—p. 1171.

Pathogenesis of "Injuries by Muscular Traction." H. Burckhardt.—p. 1174.

*Treatment of Congenital Clubfoot. H. Gardemin.—p. 1177.

Plastic Repair of Roof of Acetabulum in Coxa Valga Luxans and in Irreducible Congenital Luxation of Hip. J. Baumann.—p. 1182.

Wandering Epiphysis on Head of Femur.—Mau stresses that, if young persons, particularly boys, at about the age of puberty complain of pains in the hips, fatigue and occasional limping, the physician should take into consideration that a beginning loosening and wandering of the epiphysis might exist. It is important to recognize the beginning slipping of the epiphysis of the femoral head first backward and then downward, because the complete development of the adolescent form of coxa vara, the adduction contracture in connection with the position of outward rotation, is practically irreparable and usually leads to a deforming arthrosis of the hip, which may result in early invalidism. After discussing the normal position of the epiphysis of the femoral head and after pointing out that there are definite constitutional types that are especially predisposed to the development of adolescent coxa vara, the author discusses the pathogenic mechanism, pointing out among other factors that investigators have detected signs of softening in the epiphyseal cleft of the patients with this disorder. Moreover, in a number of cases the anamnesis reveals a mild trauma. He discusses the symptomatology and diagnosis of this condition and says that, once the "wandering" of the head begins and the femoral neck starts to turn forward, the patients generally complain of pains in the knee, and the first signs of inhibited movement in the hip joint appear. A comparison of the movements of the two hip joints usually reveals that the inward rotation as well as the outward movements of the diseased hip are restricted. A shortening of the leg is usually not perceptible during the beginning stages of the disorder, but a slight emaciation of the musculature of the thigh often appears quite early. These comparisons between the two sides are of course without value if both sides are involved. Roentgenoscopy is of great help, particularly in the obscure cases. In discussing the method of roentgenography, the author stresses that the roentgenogram made in the sagittal direction is especially valuable, in that it reveals a certain loosening and widening of the epiphyseal line. The sagittal exposure should be supplemented by a frontal one. Moreover, a pelvic roentgenogram should be taken in Lauenstein's position, for it permits a frontal exposure of the neck of the femur. Once the beginning of the epiphyseal wandering has been recognized, the author applies, without previous redressement maneuvers, a plaster-of-paris cast to the pelvic region. After four weeks he changes to a mild extension and begins with careful exercises in bed and soon thereafter with walking exercises with the aid of a splint, splinting being continued for several months. With this treatment applied to the early recognized deformity, the author obtained complete cure. He describes several cases and mentions as another important roentgenologic sign a reduction in the vertical diameter of the spherical cap of the femoral head, which appears also on the roentgenogram that is made in

sagittal exposure. He concludes his report by stressing the necessity of immediate treatment after the recognition of the early signs.

Treatment of Clubfoot.—According to Gardemin, the aim of the treatment of congenital clubfoot is the production not only of a normal external shape of the foot but also of a normal shape of the skeletal system. Only after this has been accomplished is it permissible to talk of a morphologic and functional cure. Before discussing the treatment as such, the author discusses the theoretical possibilities and requirements that must be fulfilled to accomplish this aim. He shows that it is important to treat the clubfoot as early as possible. The treatment of clubfoot, no matter at what age, follows the same principles, but the technic differs. The correction of the abnormal position does not take place in the bandage but is accomplished by molding redressements according to the method of Lorenz. The bandage is applied to preserve the correction that has been obtained. In treating clubfoot in a nursling, the author performs manual redressements every day for two weeks. He fixes the region of the ankle joint with the thumb and forefinger or with the closed fist of the one hand, so as to avoid fracture of the thin tibia and fibula. The other hand grasps the heel or the anterior portion of the foot and attempts to free the bones of the tarsus from their confined position by repeated pressure. The author does not consider it advisable to correct the malformation in one session and regards the gradual loosening of the contracted ligamentous apparatus the better method. He stresses that, in order to avoid injuries, the redressements should be done only by some one who thoroughly understands the method. After the manual redressements have effected correction, the result is fixed by means of a plaster-of-paris cast. In older children and in adults, manual correction is usually no longer possible and appliances of various types are used. The author uses the apparatus of Stille-Lorenz and of Alsberg, the Phelps-Gocht clamp and König's wedge. He does not strive to overcome the deformity completely in one session but is at first satisfied with a mild degree of correction. A plaster-of-paris cast is put on after every redressement and is left on for four weeks. The tensions within the foot may not exceed a moderate degree, or the resulting trophic changes may cause serious sequels. If redressements do not have the desired results, surgical interventions must be tried. To insure good permanent results, a careful after-treatment is essential. For a while the foot must be held in the corrected position by means of orthopedic devices, for there is danger of relapse if this is not done.

Wiener klinische Wochenschrift, Vienna

49: 1301-1328 (Oct. 23) 1936. Partial Index

*Mechanism and Therapeutic Significance of Metabolism Increasing Action of Dinitrophenol Derivatives. H. Handovsky.—p. 1301.
Methods of Investigation of Human Heredity. Berta Aschner.—p. 1304.
Individual and Superindividual Aims in Psychotherapy. H. Kogerer.—p. 1307.
Disputed Questions in Acute Necrosis of Pancreas. R. Demel.—p. 1309.
*Carcinoma of Small Intestine with Chronic Invagination: Case. E. Knirsch.—p. 1313.
Thyroptotic Pseudo-Angina Pectoris. S. Kreuzfuchs.—p. 1314.

Dinitrophenol Derivatives.—In a review of the history of dinitrophenol derivatives, Handovsky points out that the attention of toxicologists has been directed to these substances because they have been used for the coloring (yellow and orange-red) of foods for approximately five decades. As early as 1885 it was found in animal experiments that the ingestion of these substances may result in polypnea and increased temperature. The first knowledge about the localization of the action of these substances was obtained through investigations on the toxicology of 2-4-dinitrophenol, large quantities of which were used in French gunpowder factories during the World War. These investigations were carried on because of numerous cases of poisoning among the workers of these factories. In later years the studies were continued and, as regards the localization of the action of the dinitrophenol derivatives, it was found that in several species of animals there was a considerable increase in loss of heat by polypnea and sweats, a rise in temperature and an enormous increase of the metabolism, of the loss of glycogen and of the oxygen consumption. Later experiments revealed that the dinitrophenol derivatives have no central point of attack and that the heat production effected by dinitrophenol takes place in the muscle cells. Thus the action of these substances is a cellular one. The author cites the studies of other investigators and then states that he himself was able to prove that the dinitrophenol derivatives are capable of stimulating the dehydrogenation processes. He describes and discusses experiments from the outcome of which he concludes that the dinitrophenol derivatives increase the metabolism and the temperature by stimulating the combustion of substances with a high combustion heat. These substances are formed in the organism even under normal conditions, but ordinarily their caloric value is not being utilized. Because the dinitrophenol derivatives facilitate the combustion of body materials, attempts were made to use them in the treatment of obesity. However, it was discovered that medication with dinitrophenol involves many dangers and so the therapeutic use was discouraged. Nevertheless, the author thinks that experimental therapy should make further studies on the dinitrophenol derivatives. It should be investigated whether their capacity to prevent the division of cells might be of value in the treatment of cancer. Moreover, they might prove helpful in irradiation and in fever therapy. In the treatment of obesity the combination of subtherapeutic doses may prove helpful.

Carcinoma of Small Intestine with Chronic Invagination.—Knirsch, after pointing out that cancerous degeneration of the small intestine is not as rare as was formerly believed and after citing statistics about the incidence of this form of cancer, reports a case of primary cancer of the small intestine, which is noteworthy because the cancer resulted in chronic invagination. Moreover, in spite of the fact that the patient had diabetes and a myocardial defect, the invagination tumor could be radically removed in a single operation and the patient could be discharged as cured.

Polska Gazeta Lekarska, Lwów

15: 789-808 (Oct. 11) 1936

Malignant Tumors. J. Jasieński.—p. 789.
*Congenital Disposition to Malignant Tumors. N. Pende.—p. 793.
Action of "Pituspasmine" and of Parturient Women's Serum on Uterine Muscles. S. Boguszewski.—p. 797.

Congenital Disposition to Malignant Tumors.—Pende says that in malignant tumors there is a dynamic-humoral condition of the entire body or of special organs which predisposes the tissues to the development of malignant tumors under the influence of external causes but which alone would not be sufficient for the development of a tumor. Experiments on both human beings and animals disclose various causes, but the natural cause has not been proved. Cancer is a constitutional disease and local treatment by surgery or other means is a mistake. He points out that the Irish and the Basque are especially predisposed to cancer, while the Negro and the Indian are seldom affected by malignant tumors, and he feels that the amount of intake of cholesterol may have some influence in the matter. However, he thinks that it is unwise at this time to give any cause for the predisposition to cancer for the different races. Heredity is an important factor, as is sex, since women are more often affected than men. Age should also be taken into consideration. Finally, there does not seem to be any doubt that there must be some relationship between the various endocrine glands and cancer, such as between cancer of the stomach, the skin and the intestine and overactivity of the thyroid and vagotony and tumors of the female organs, with hyperactivity of the anterior part of the hypophysis.

Problemy Tuberkuleza, Moscow

Pp. 1203-1338 (No. 9) 1936. Partial Index

Histogenesis of Tuberculous Inflammation. G. E. Zeman.—p. 1204.
Histogenesis of a Tubercle. M. G. Ivanova.—p. 1210.
*Pathologic Anatomy of Dust Tuberculosis. I. I. Moshkovskiy.—p. 1218.
Lung and Metabolism. S. M. Leytes.—p. 1226.
Sources and Modes of Development of Pulmonary Tuberculosis. B. M. Khmelnitskiy, M. Ya. Karliner and K. A. Pushkar.—p. 1232.
Method of Determining Functional Capacity of Cardiovascular System in Pulmonary Tuberculosis. A. E. Rabukhin, A. I. Gurevich and L. A. Spivak.—p. 1246.

Pathologic Anatomy of Dust Tuberculosis.—On the basis of an investigation of 2,600 miners of the Donbass region, Moshkovskiy concludes that pneumoconiosis exists as an inde-

pendent disease entity. Clinical, roentgenologic and biologic data obtained over a long period demonstrated that a preponderant majority of cases of pneumoconiosis were not tuberculous. He feels justified in dividing his cases into those of pneumoconiosis caused exclusively by dust, and those of coniotuberculosis in which both factors exist—dust and tuberculous infection. Clinical, pathologic and histologic studies of his cases fail to support the hypothesis that the nonspecific fibrosis resulting from coniosis can act as a defensive mechanism against a tuberculous infection. Postmortem examinations of several of his cases demonstrate the possibility of development of a grave tuberculous process with caseous tissue reaction on a basis of intensive coniotic fibrosis. This concept of a mechanical blockade is further contradicted by the localization of tuberculous caseating foci in the center of coniotic areas. Peribronchial and perivascular distribution of purely coniotic areas without elements of tuberculous infection was likewise found. This testifies to pneumoconiosis as an independent process. The pneumoconiosis node differs from the tuberculous focus by the absence of lime and central necrosis. Tubercle bacilli in sputum are less frequent in coniotuberculosis even in the presence of considerable destruction of the pulmonary tissue, probably because of limited connection between cavities and the bronchi. Coal pigment spreads by way of lymph and blood and in advanced cases may be seen deposited in the various viscera, particularly the liver and spleen.

Finska Läkaresällskapets Handlingar, Helsingfors

79: 667-754 (Aug.) 1936

Examination of Perception of Color in Applicants for Positions in Transportation Service. O. Heinonen.—p. 667.
*Bone Marrow in Hemolytic Jaundice, Together with Contribution to Question of Nature of Megaloblasts. G. Tötterman.—p. 686.
*Treatment of Lichen Ruber Planus (Especially with Roentgen Irradiation and with Injections of Bismuth): Comparative Investigation on Results. C. E. Sonck.—p. 702.

Bone Marrow in Hemolytic Jaundice.—In Tötterman's case of hemolytic jaundice, the patient being a woman aged 33, treated in 1935, liver therapy proved ineffective, succeeding treatment with arsenic for several weeks was without marked effect, but splenectomy was followed by rapid improvement. The first sternal puncture, shortly after admission, showed 1,893 nucleated red blood corpuscles per 400 white corpuscles; there were 1,217 normoblasts, 470 macroblasts, twenty-two normoblasts with mitosis, 110 normoblasts with amitosis, twenty macroblasts with mitosis and one mature megaloblast, together with fifty-three large cells with nongranulated basophile plasma and a round, finely reticulated nucleus with two or three nucleoli. As in the blood, the number of reticulocytes in the bone marrow was 0.6 per cent. On the second sternal puncture, about three weeks later, there were 259 normoblasts, sixty macroblasts, two normoblasts with mitosis, three macroblasts with mitosis, and seven promegaloblasts. A third sternal puncture, seven months after splenectomy, when the blood had been normal for a considerable time, except for the continued lowered resistance and microcytosis, revealed a normal white blood picture with ninety-nine normoblasts, five macroblasts, five macroblasts with mitosis and one uncertain promegaloblast to each 400 white cells, affording further proof of the effectiveness of splenectomy in hemolytic jaundice. In this case both the mitotic and particularly the amitotic erythropoiesis in the bone marrow was more pronounced than in any case of pernicious anemia. The patient was not achylic and apparently had all of Castle's "intrinsic factor," which protected her against a disturbance in the maturing process of the erythroblasts, so that mainly normoblasts and normocytes developed.

Treatment of Lichen Ruber Planus.—Sonck states that of seventy-three patients presenting lichen ruber planus given roentgen treatment, 42.5 per cent recovered, 35.4 per cent improved and in 21.9 per cent the results were negative. Of twenty-nine treated with a bismuth preparation 38 per cent recovered, 41.4 per cent were improved and 20.7 per cent were unchanged. Of seventeen treated with arsphenamine, 29.4 per cent recovered, 41.2 per cent were improved and 29.4 per cent were unchanged. Bismuth is cheaper than arsphenamine, more convenient and, properly given, is safe. Especially for patients who do not bear treatment with arsenic and for whom roentgen therapy is not available, attempted treatment with bismuth compounds is advocated. Improvement sometimes appears slowly. Some cases prove resistant. On the whole, recent cases seem more amenable to roentgen and bismuth treatment than older cases.

Upsala Läkareförenings Förhandlingar, Uppsala

42: 1-207 (July 1) 1936

New Points of View on Early Embryonal Development. D. E. Holmdahl.—p. 1.
Contribution to Question of Development of Premature Children Up to First Years of School. Gert von Sydow.—p. 21.
*Hyperparathyroidism with Multiple Thrombi: Case. J. Mellgren.—p. 35.
External Kidney Pelvis: Compilation from Literature and Two Personal Cases. P.-E. Enbark.—p. 47.
*Influence of Dinitrophenol 1-2-4 on Tar Cancer in White Mice. K. A. Vannfält.—p. 55.
*Pointing Test: Test of Some Hypotheses for Its Clinical Applicability. W. Behrman.—p. 67.
Continued Investigations on Occurrence of Vitamin D in Baltic Herring. G. Blix and Gösta Englund.—p. 203.

Hyperparathyroidism with Multiple Thrombi.—In Mellgren's patient, a woman aged 41, previously well, there was sudden onset of continued vomiting and exhaustion, slight infection of the upper respiratory tract, fever and increased sedimentation, with signs of slight kidney disturbance and marked and increasing leukocytosis. Pain in the back appeared and death occurred after two weeks, with a picture of paralysis of the heart. Necropsy showed an enlarged parathyroid gland and calcium deposits in the heart and kidneys, together with multiple recent thrombi in the kidneys and lungs. From experimental results cited the author concludes that the parathyroid extract increases the coagulation ability of the blood as well as its calcium content, and the thrombi in this case are thought to be related to the parathyroidism.

Influence of Dinitrophenol 1-2-4 on Tar Cancer.—Vannfält's results afford no evidence that dinitrophenol 1-2-4 in the dosage of 10 mg. per kilogram of body weight daily or from 10 to 20 mg. every second or third day affects the development of tar cancer in mice.

Pointing Test.—Behrman's study of spontaneous pointing in normal persons supports the view that the results depend largely on the method applied. Of eleven methods tested, only three are characterized as new. He finds that, in the methods in which the arms approach their aim during an upward movement, the arms deviate outward from the median line; these methods give more marked results after irritation and the effect is increased when no correction is made after each pointing and is further heightened by simultaneous pointing with both arms. In method 10, belonging to this class, in his opinion the best method, there is an average deviation of 3.79 + 0.08 (0.25) cm. for the right arm and 3.33 + 0.08 (0.25) cm. for the left arm. The deviation from the variation field of spontaneous pointing increases after calorization, reaching the maximum at about the tenth pointing. Irrigation of one ear with cold water affects the arm of the opposite side, irrigation with warm water the arm of the corresponding side. The caloric test with 100 cc. of warm water causes a stronger reaction than the test with 5 cc. of warm water; the test with cold water results in a more marked reaction than that with warm water, although the difference with regard to the body temperature is the same in the two cases. The deviation in the first pointing to a certain extent determines the deviations in succeeding tests. A table is given for use in determining whether the patient points spontaneously inside or outside the limits of the variation width in normal persons, and for determining whether or not a given vestibular irritation affects the pointing arm. The author asserts that by application of his method about two thirds of the cases react at least in one arm after irrigation of an ear, and two thirds of the persons in whom one irrigation causes no reaction in an arm react when the other ear is irrigated once. After rotation with ten revolutions within ten seconds there is a 93 per cent probability of obtaining some irritation reaction. The diagnostic effect of pointing can be increased by repeated irritation tests. No certain relation between dizziness and pastpointing was established.